DECEMBER 1950

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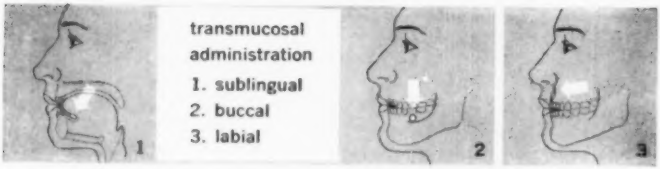

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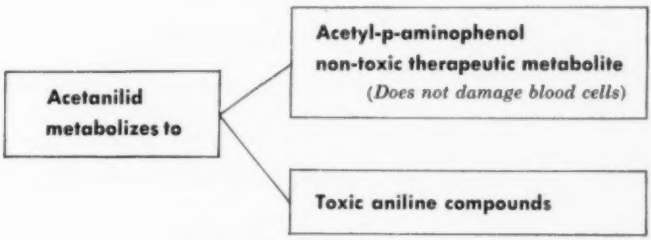

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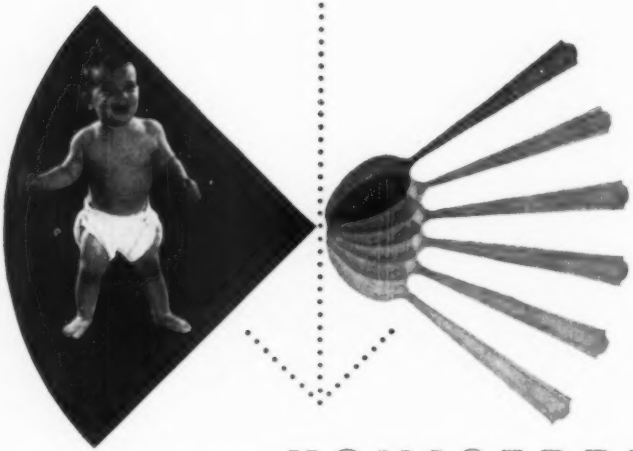

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SECOND SERIES DECEMBER 1950 VOL. 26, NO. 12

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BULLETIN OF
THE NEW YORK ACADEMY
OF MEDICINE

VOL. 26, NO. 12 DECEMBER 1950

OPENING ADDRESS

Twenty-third Graduate Fortnight*

Benjamin P. Watson

President, The New York Academy of Medicine

On behalf of The New York Academy of Medicine I bid you welcome to its 1950 Graduate Fortnight.

The Fortnight was instituted twenty-three years ago and each year since some aspect of medical science and practice has been reviewed. I trust that this year you will find the program provided as stimulating as have been those in the past.

It takes much knowledge, thought and planning to decide on a major subject for discussion and to have it presented in its various subdivisions by those best qualified to speak. This task is undertaken by the Committee on Medical Education of the Academy acting through a small subcommittee specially selected for the purpose.

The names of the members of this subcommittee with Dr. Currier McEwen as Chairman and Dr. Mahlon Ashford as Secretary appear in your folders. I take this opportunity of conveying to them the thanks of the Academy for their work and effort. I also wish to thank all those who have so readily acceded to our invitation to take part in the program. Some of these are our own Fellows whilst others are distinguished scientists and clinicians working in medical schools and institutions situated throughout the length and breadth of the North American Continent.

* Given October 9, 1950 at The New York Academy of Medicine.

This year's program deals with diseases and disabilities affecting the Musculo-Skeletal System. Whilst most of these are not serious so far as an immediate threat to life is concerned, many of them are attended by such loss of function as to render the victim incapable of full physical activity or of earning a livelihood. With our aging population the numbers suffering from these disabilities is increasing, so placing an added strain on our whole economic system. The problem of prevention and treatment is thus not only individual but national in its implications.

The so-called rheumatic diseases alone take a heavy toll on our population. It is in the understanding and treatment of these and allied conditions that the most spectacular scientific and clinical advances have been made in recent years. You will have the opportunity in the evening lectures of hearing from those who are pioneers in this advance and have been putting scientific facts to clinical application. They will tell us where we stand at the present time and what are likely to be the developments in the future. These developments will depend upon a more complete understanding of the structure of and the physiological and pathological processes occurring in connective tissue, muscle and bone. This aspect of the problem will be dealt with by speakers who are actively engaged in its elucidation.

When irreversible changes have occurred in muscle, joint or bone the orthopedic surgeon can now step in and by many ingenious procedures improve or restore impaired or lost function. Notable advances have been made in the rehabilitation of those suffering from muscular, arthritic and skeletal disabilities. These and other subjects will be dealt with in the Morning Panel Discussions.

At the afternoon Hospital Clinics opportunity will be given to see patients suffering from the various lesions, some in the course of active treatment, some undergoing rehabilitation and others cured, improved or in statu quo.

The Scientific Exhibit on the first two floors of this building is open from 10:30 a.m. to 10:30 p.m. Dr. Alfred Angrist and the contributors have gone to a great deal of trouble to make it of true educational value and I commend it to your attention.

Miss Doe, our Librarian, and Miss Annan have set out a collection of books, articles and atlases dealing with the conditions under discussion.

Motion picture demonstrations and televised surgical operations complete the program. We hope that you who take part in it will find it rewarding.

SKELETAL CHANGES ASSOCIATED WITH DISEASES OF THE BLOOD*†

MARCY L. SUSSMAN

Clinical Professor of Radiology, University of Southern California School of Medicine

Wesley M. Carpenter Lecture

It has not been easy to prepare a talk being conscious always of the august tradition of this Lecture which honors Dr. Wesley M. Carpenter. My predecessors have set high standards which I cannot hope to emulate. My briefing instructions were to present the significant advances in the subject of skeletal lesions associated with diseases of the blood. Time requires that I limit my discussion to the changes in leukemia, in myelosclerosis and in the chronic familial and racial anemias. I shall review the roentgen appearance of these bone changes, but I hasten to say that, although through the kindness of radiologists in many parts of the United States, I have been privileged to study a large amount of radiographic material, I have nothing to add to the descriptions you will find in many textbooks. During the past two years, however, it has become apparent that in certain instances of these incurable diseases, the bone lesions may be altered and the bone structure return to a near-normal appearance. These findings, and other recent literature, justify speculation regarding the pathogenesis of the bone changes which I propose to do even though there may be many in this audience whose wider experience will find what I have to say unacceptable.

LEUKEMIA

The bone changes in leukemia are not uniform but perhaps that is, in part, a reflection of the fact that leukemia is not in the biological sense a uniform disease. For example, acute leukemia generally occurs in children. Acute cases also occur in elderly adults but it is thought by some

* Given October 12, 1950 before the 23rd Graduate Fortnight of The New York Academy of Medicine.

† The papers presented at the 23rd Graduate Fortnight of The New York Academy of Medicine will be published in book form by The Macmillan Company, New York.

that they are acute exacerbations of chronic disease. Chronic lymphocytic leukemia usually appears over the age of fifty years. The age spread in acute and chronic myeloid leukemia is somewhat more uniform but the acute disease usually occurs in the first decade. There are other significant biologic differences between lymphocytic and myelocytic leukemia and between the acute and chronic diseases which are reflected in such biochemical features as the beta-glucuronidase level of the buffy coat,[1] the total blood histamine levels[2] and the carbonic anhydrase activity of the peripheral leukocytes.[3] The response of individual cases to various drugs is not uniform and we shall have occasion to speak more of this later.

In acute leukemia, the growing skeleton is affected in nearly all cases unless early death supervenes.[4] Skeletal changes are demonstrable radiographically in more than one-half of leukemic children.[5, 6] Four types of roentgen change are seen.[5] Most often, there are transverse bands of diminished density in the metaphyses of the long bones, sometimes sharply defined, sometimes indefinite and merging with normal bone. The knees are the most convenient area to look for these changes. Occasionally a uniform transverse band progresses into a grossly irregular and apparently osteolytic lesion but the transition is not a sharp one. It is not unusual for both types of lesions to be present in the same case. Osteolysis may be both focal and diffuse. The focal form is characterized by areas of translucency in the spongiosa which may be confluent. The involved bone may appear motheaten and suggests destruction of both the spongy and compact bone. Not infrequently there are spontaneous fractures. Rarely there is a generalized decalcification of the entire skeleton.

Osteosclerosis is not uncommon occurring in about 10 per cent of the acute leukemics. The endosteal new bone formation is thought to be due to overproduction of cancellous bone rather than to thickening of the cortex. Often there are patchy conglomerate areas of increased density which may be quite marked. Lifting of the periosteum, periosteal thickening and irregular new bone formation is more frequent and is found in perhaps one-fifth of the acute cases. Cortical thickening has been observed in all of the major long bones, less frequently in the ribs and the small tubular bones of the hands and feet. In advanced cases, spotty destruction is visible in the larger epiphyseal ossification centers and in the flat bones of the calvarium, shoulder girdle and pelvic girdle. When an

epiphysis and juxta-epiphyseal portion of a bone are involved, aseptic necrosis may be simulated.

In chloroma, localized masses are found most often in relation to the periosteum and ligamentous structures particularly of the skull, paranasal sinuses, orbits, spine, ribs and sacrum. Periosteal changes are found in addition to those in the medulla.

In chronic leukemia, occurring in the adult, the lesions usually appear destructive although an occasional example of osteosclerosis has been reported (I am excluding for the moment the cases of myelosclerosis who die with leukemia). By the time the patient is subjected to radiographic examination, the lesions are usually multiple. Discrete or confluent areas of rarefaction are found, resulting in a motheaten appearance. Vertebral compression is a relatively frequent finding. Innumerable areas of osteolysis in the skull involving the diploe or diploe and cortex are not infrequent. Periosteal elevation is fairly common. The most frequent sites of involvement are the femurs and humeri as well as the pelvis and spine. Radiographic abnormalities are said to be present in about 8-10 per cent of chronic leukemics[7] but this figure may be misleading because many patients are not referred for roentgen examination.

Pathology: I am not competent to discuss in any detail the pathology of leukemia. You know that both myelocytic and lymphocytic varieties involve the bone marrow, lymph nodes, spleen and other pre-existing lymphoid tissues. Heterotopic growths of lymphoid tissue appear in the liver, kidney, lung, skin, serous membranes and many other organs. Of particular interest, however, is the fact that in most cases, the aggressive quality of cancer is lacking, as Ewing[8] points out in the following words: "In the bone marrow, the process begins in multiple hyperplastic foci which enlarge, coalesce and eventually extend the limits of lymphoid marrow throughout all portions of the skeleton. At the height of the process the new tissue is firm, light-colored, opaque or pyoid, or beset with foci of infarction, necrosis, hemorrhage or mucoid softening . . . the spongy trabeculae are often absorbed and even the shafts may be thinned but a distinctly aggressive destruction of bone as in true tumor is missing. . . . In acute febrile leukemia, local aggressive properties are almost entirely wanting, the infiltrating cells show a great respect for the invaded tissues, the lymph node lesions may be very moderate, local lymphomas may be scanty, and any neoplastic quality present is confined to the simple multiplication of atypical cells, while an acute toxic

process is prominent. In chloroma, on the other hand, a very different grade of neoplastic properties is present, and the effects are so different that it seems unwarranted to exactly identify the two processes."

It would seem then that the bone rarefaction which we see in leukemia is not ordinarily explained by an aggressive destruction of bone. We can account for thinning and destruction of bone trabeculae in many cases by pressure, hemorrhage, necrosis and infarction, resulting from crowding of the closed marrow spaces with leukocyte-forming tissue.[9] This has been suggested as the reason the roentgen changes in adults are less pronounced than in children. The bone marrow space in infants and children is completely or largely occupied by hematopoietic tissue, whereas in adults, much of the marrow has become fatty and there is room for expansion. However, this mechanical theory fails to explain many of the roentgen and correlated pathological features. The following are some of these discrepancies.

(a) There is general agreement that the transverse metaphyseal zone of diminished density is not seen exclusively in leukemia. It is found in a variety of conditions and in apparently normal children. It was observed in Nagasaki where it was thought to be due to radiation and malnutrition.[10]

(b) The skeletal lesions appear and disappear rapidly. X-ray evidence of bone involvement may appear within four to ten weeks after the onset of symptoms. This perhaps is not surprising when it is recalled that a transition from a completely fatty to a solidly cellular marrow has been seen under experimental conditions within two days.[11] However, the speedy reossification which may follow the administration of folic acid antagonists in acute leukemia is less readily explained on purely morphologic grounds. Karpinski[12] refers to a case in which there is evident beginning reossification of osteolytic areas in the shaft of the radius six days after instituting treatment. This change was apparent in the "destroyed" compacts as well as in the cancellous portion. Transverse metaphyseal bands of diminished density were observed by Silverman[13] to disappear within four to six weeks of this therapy. The rarefied zone is replaced first by a fine line of increased density which, in time, presents as a heavy transverse band. Dr. Silverman has been kind enough to let me see his cases but I can add nothing to his description as follows: "as this band widens, it loses some of its density between the epiphyseal and diaphyseal faces of the band. Gradually two parallel lines are

formed, one deep in the shaft, the other at the epiphyseal plate. The line in the shaft becomes more deeply buried as longitudinal growth of the bone carries the epiphyseal plate away from the region, and the epiphyseal plate again widens and undergoes the same cycle of change." Histologic examination of the bone in such cases demonstrates "an increase in the number and thickness of trabeculae in the region of the transverse line and a persistence of a homogenous gray-blue-staining material as a central core beneath the newly formed bone." There are many well-documented instances, some in my collection, of the disappearance of the transverse bands and other apparently osteolytic lesions during spontaneous clinical remission. It is curious, however, that I have been unable to find any reference to similar alterations following treatment with nitrogen mustard, urethane or other presumably cytotoxic drugs. If any have occurred, they must be few. This is due, at least in part, to the fact that these drugs are not ordinarily clinically effective and are now seldom used in acute leukemia. ACTH, however, is said to produce clinical remissions in a few instances,[14] but I have found no reference to the regression of a bone lesion. I found only one mention[15] of this result following a systemic agent other than a folic acid antagonist, namely "in a case of acute leukemia, the roentgen appearance of lumbar and dorsal vertebral destruction was improved after P_{32} therapy." Local roentgen therapy to an involved bone in chronic leukemia may result in repair of the lesion but precise information about the mechanism is not available.

(c) In twelve patients of the series reported by Karpinski and Martin,[15] there were chest lesions, including hilar adenopathy, pleural effuson and parenchymal disease, none of which was influenced by aminopterin. However, some of these children exhibited bone lesions which did respond. I interpret this to indicate that the bone changes may have a unique pathogenesis, although other explanations are possible.

(d) The use of folic acid antagonists in the treatment of leukemia followed the observation that folic acid seemed to stimulate the leukemic process.[16] There can be little doubt that both folic acid and its antagonists have a profound effect both on the leukemic process and on normal tissue, but whether the difference is qualitative or quantitative is not yet clear. However, the fact that aminopterin therapy has resulted in the disappearance of bone rarefaction in 20-30 per cent of cases of acute leukemia suggests that not only is the leukemic process modified

but also bone formation. This assumption is strengthened by the finding that areas of bone rarefaction which reossified during a clinical remission induced by aminopterin, reappeared during the continued administration of this drug even though there was no change in the clinical and hematologic status.[15, 17]

The discrepancies have led me to a hypothesis regarding the pathogenesis of at least some of the skeletal lesions which I will present to you even though I have no corroborative experimental data of my own. Published data suggest that the rapidly growing immature granulocytes are capable of fixing or utilizing an excessive amount of folic acid.* I suggest that there is created thereby a relative deficiency of this substance in other metabolic functions. There is no direct proof of this theory but it would provide a satisfactory explanation of the macrocytosis which is found in some cases of leukemia and which heretofore has been assumed to be due to a mechanical or toxic factor.[19]

When aminopterin is administered, it may be accepted by the rapidly metabolizing leukemic cells in place of folic acid. There is experimental evidence supporting this thought.[20] The folic acid freed from utilization by the leukemic cells might now be available to correct the deficiency which I assumed to be present in other tissues. With continued therapy, the increased leukemic requirements being met by aminopterin are reduced as the number of immature cells is reduced. Part of the administered aminopterin is now freed and enters successfully into competition in the enzyme systems of normal tissue. It is important to recall in this respect that the basic feature of the action of competitive antagonists is that the velocity of the enzymatic reaction is proportional to the ratio of the concentrations of metabolite and antagonist rather than to the concentration of one alone.[21]

I do not know what part, if any, folic acid plays in bone metabolism. It is said to be essential to the normal functioning of all cells. However, it might be significant that vitamin B_{12}, which appears to be closely related to folinic acid in its actions, apparently is involved in the methylation of hemocystine to methionine and in the reduction of cystine to cysteine.[22] These are "free" essential amino acids of which there are no reserve stores in the body. In their absence, a deficiency in a particular one cannot be corrected from the protein stores themselves. These

* Folic acid is used to mean the acid itself or a utilizable derivative. Folinic acid might be more properly used since this is now thought to be the utilizable form of folic acid, and folic acid antagonists may operate by interfering with the conversion of folic acid to folinic acid.[18]

amino acids are essential for growth and are intimately involved in the protein substrate of maturing bone but whether their deficiency creates a specific lesion or the non-specific lesion of malnutrition is not known. Malnutrition is known to interfere with osteogenesis. The epiphyseal cartilage stops proliferating and bone growth ceases at the cartilage shaft junction and in the shaft as well.[23] However, Silverman noted that there is no significant retardation of longitudinal growth during aminopterin therapy.[13] Another possible link is the finding that the excretion of folinic acid in humans depends on the ascorbic acid levels.[18] Furthermore, Hagtvet[24] found low, almost undetectable levels of ascorbic acid in the serum of leukemics. The latter finding, however, may be a non-specific result of a febrile disease.[2] Dr. E. Neuhauser whose data I have quoted,[17] wrote me that he believes that there is an antagonistic action of the aminopterin with some substance that has to do with intercellular cement formation or matrix formation. Perhaps he is wise to venture no further than this in speculating on mechanisms.

A discussion of leukemia would be incomplete without some reference to multiple myeloma. It is possible, perhaps, probable, that this disease is a variant of plasmocytic leukemia such as lymphosarcoma is thought by many to be of lymphocytic leukemia. Snapper[25] cites excellent reasons in support of this view. Wintrobe[26] also quotes pertinent cases. However, because our time is limited and because, in spite of marked clinical palliation which may follow treatment with stilbamidine and urethane, there have been few reports describing an alteration in the skeletal lesions, the subject will not be discussed in the present review.

Myelosclerosis with Leukoerythroblastic Anemia

Diffuse fibrosis of the bone marrow is an unusual progressive condition which sometimes follows a known disease or intoxication but often develops without known cause. Occasionally, there is in addition proliferation of cancellous bone but, as far as can be determined, this is not the result of a fundamental difference in the two processes. Clinically, the syndrome is that of myelophthisic anemia. There may be a leukoerythroblastic peripheral blood picture but more often there is leukopenia. Preterminally, a marked increase in the number of granulocytes may be found.

At autopsy, myeloid proliferation characterized by the predomin-

ance of megakaryocytes, is present in the spleen and to a less extent in the liver. The bone marrow of long bones, skull, vertebrae, pelvis, ribs and sternum shows a uniform change. Early, all of the marrow may be deep red, moist and succulent; it appears markedly hyperplastic. Later, the bones are uniformly dense, grey-white and hard without any well-defined marrow spaces, or may show scattered foci of red or yellow marrow.[27] In the early stages, both the myelopoietic and erythropoietic elements are increased. Eosinophilic myelocytes as well as mature and immature megakaryocytes stand out and appear to be increased in number. There are also cells which seem to correspond to stem cells of undetermined nature. There is evidence of necrobiosis of many immature cells which lie in the midst of visible marrow. The marrow reticulum cells are increased in size and number and form complete septations.[27]

Later in the disease, marrow atrophy appears. The marrow reticulum is more prominent and islands of active blood cell formation are few. The loose network of reticulum is filled by a finely granular or vacuolated material resembling coagulated protein-containing fluid; at other times, collagen formation is simulated. There are numerous dilated empty vessels surrounded by small groups of bizarre megakaryocytes or small hematopoietic cells. The end stage in a certain number of cases involves a distinct type of new bone formation[27] which is of particular interest in our present discussion. There are first focal granular deposits of calcium in the eosinophilic matrix where reticulum cell nuclei lie parallel and close to a trabecular surface. After the matrix is calcified, bone is deposited in a layer about part or all of the old trabecular surfaces. Prominent cement lines permanently demarcate the margins of the original trabeculae. This process becomes generalized but irregular and the eventual trabecular pattern is quite tortuous with jutting, rounded thickenings of spongy bone. Ultimately, completely new bone trabeculae, which are irregular in thickness and direction, are formed in the marrow spaces by precipitation of calcium in the fluid or gelatinous reticular matrix, with an intermediate osteoid stage.[27]

In this later stage, roentgenologically, the usually sharply defined trabecular structure gives way to an overall ground glass appearance. There may be a uniform increase in density or more patchy areas of condensation. Not infrequently, scattered more or less uniformly through the dense bone are small, rounded areas of relatively diminished density. The cancellous bone appears particularly to be affected. The

compacta may be broadened but is not as dense; it sometimes seems relatively porotic. The distribution of lesions radiographically corresponds to that described pathologically. The changes are not pathognomonic but when found in association with a very large spleen, will permit the roentgenologist to suggest the diagnosis.

Fibrosis and even sclerosis of bone marrow with myeloid metaplasia in spleen and liver is found in many conditions including such varied diseases as marble bone disease, acute tuberculosis[28] and metastatic carcinoma. The relation to certain other coincident or antecedent diseases particularly leukemia has been the subject of considerable debate. Occasionally the myelosclerotic patient dies with what competent pathologists consider to be true leukemia.[25] Two of my cases were in this category.[29] Custer[11] refers to a characteristic case with early bone marrow hyperplasia and typical granulocytic leukemia. Two years later, there was bone proliferation and partial fibrosis of the marrow. Seven years later, at autopsy, all bones were densely sclerotic. Other reports, however, state unequivocally that "myeloid metaplasia . . . is of a fundamentally different nature than leukemia."[30] Leukemia cannot be excluded in the individual case except at autopsy and even then the diagnosis often rests on a personal interpretation of the morphology. There is unfortunately no biologic test for the disease. Perhaps the observation that the total blood histamine is elevated in chronic granulocytic leukemia and is normal in physiologic leukocytosis and leukemoid reactions[2] will provide useful additional data.

Many cases of myelosclerosis follow "burnt out" polycythemia. The bone marrow picture in this disease is complicated by the fact that the patients have almost always been subjected to irradiation, phlebotomies and later, transfusions. Some authors believe that at least some instances of polycythemia represent a response to early leukemic infiltration of bone marrow. An interesting observation in this connection is the finding that the total blood histamine is elevated in chronic myelocytic leukemia and in polycythemia.[2] A recent review of the literature emphasizes the significant result that with one exception, all cases of polycythemia which become leukemic had been exposed to some form of irradiation.[31] The observation that a sustained increase in erythrocyte counts occurs in patients treated for more than two weeks with ACTH or cortisone led Thorn[32] to suggest a possible role of cortisone-like hormones in the pathogenesis of polycythemia. Should this theory prove to

have merit, the delayed and inconstant appearance of myelosclerosis in this disease might be related to the protective action of hyperadrenal corticoidism on connective tissue.[33]

It is evident that there is little precise information regarding the pathogenesis of this skeletal abnormality. The fact that the disease is known by so many names expresses the confusion regarding its fundamental nature. It is unlikely that mechanical limitation of hematopoietic tissue is a primary factor since, as Vaughan pointed out, the total quantity of red marrow is often quite in excess of the amount normally present.[34] It is not clear whether osteosclerosis is the result of a simultaneous stimulation of derivatives of the primitive mesenchyme reticulum cell—osteoblasts, fibroblasts, hematocytoblasts and megakaryocytes —or is secondary to another disease. Wyatt and Somers[27] for example discussing chronic marrow failure implicate as etiologic factors, exogenous toxic chemicals, endocrine abnormalities, blood loss or destruction and cardiovascular disease. They suggest that pathogenesis is by way of liver dysfunction which results in protracted marrow exposure to certain substances normally conjugated rapidly in the liver and excreted. Others regard myeloid metaplasia as a non-specific response of immature multipotent cells of the liver and spleen to a wide variety of stimuli,[30] and osteosclerosis as a further secondary phenomenon.

It seems to me significant that unusual numbers of osteoblasts or osteoclasts are not present in the osteosclerotic marrow. This might suggest that primarily there is a physico-chemical change in the protein substrate of bone with altered conditions for the precipitation of calcium. If my discussion of the pathogenesis of the leukemic bone changes merits consideration, there is the possibility of applying a similar analysis to our present problem. We have seen that the continued administration of a folic acid antagonist to a leukemic in clinical and hematologic remission results in the reappearance of rarefaction in the metaphysis. It is also reported that in leukemic marrows, a diffuse fine fibrosis results from chronic exposure to folic acid blocking agents.[35] Although myelosclerosis is the characteristic bone change in myeloid metaplasia extensive decalcification has been noted in a medullary form of aleukemic myelosis described by Bouchut, Levrat and Guichard.[25] In this syndrome there is a proliferation of erythroblasts, myeloblasts and megakaryocytes which is strictly limited to the bone marrow. In the parts of the skeleton where the marrow shows abnormal proliferation the cortex of the bone is

thinned and is porotic. It is not too difficult to imagine that in the usual case of myelosclerosis, similar alterations take place in the bone matrix but with physicochemical conditions such that excess rather than less calcium is precipitated.

Chronic Familial and Racial Anemias

This group of anemias includes those diseases in which there is a congenital dystrophy of erythropoiesis. There is an excessive destruction of red blood cells but to a varying degree in the different diseases. The present discussion will be limited to familial hemolytic jaundice, sickle cell anemia and familial erythroblastic anemia. All of these conditions are transmitted as a mendelian dominant trait, appearing in a major form when homozygous. The trait is present at birth but may never become clinically evident. On the other hand, active manifestations may appear at any age. Common to all three conditions is a markedly hyperplastic marrow.

There are skeletal changes which ordinarily are thought to result from the overgrowth of the marrow causing dilatation of the medullary cavity and pressure atrophy of the spongiosa and corticalis.[4] The radiographic appearance suggests to me that there is a preservation and exaggeration of the fetal type of bone formation but proof is lacking. Developmental anomalies also appear. These bone changes are frequent in the erythroblastic anemia of childhood, less common in sickle cell anemia and relatively uncommon in hemolytic jaundice. No basic difference in the patterns has been described. The variation between the bone lesions in the three diseases seems to be one of frequency, severity, extent and distribution. On the other hand, in a given disease there is no absolute correlation between the degree of skeletal abnormality and clinical severity. Excellent descriptions of the x-ray changes have been given by Snapper[25] and Caffey.[4] The following is in general a summary of their chapters.

In Cooley's anemia, there is a generalized spongy osteoporosis. The proliferation of the marrow first involves the cancellous bone, then the cortex. In the calvarium, the tables are more widely separated than normal due to broadening of the diploic space. The outer table in particular becomes atrophic but the total thickness of the bone is increased. Later bone trabeculae develop at right angles to the tables and perforate the outer table giving rise to the hair-on-end appearance.

Caffey considers that the radial appearance is probably a compensatory arrangement to support the diploic space in the presence of a weakened atrophic outer table. The frontal bones thicken first; the process then spreads to the parietal and lastly to the occipital bones. Even when the skull is markedly thickened and striated, the nasal process and the lower portion of the frontal bone remain free of striation. The air spaces in the temporal bone and the paranasal sinuses are encroached upon by the swollen contiguous bones and may be obliterated. Swelling of the zygomas makes the cheek bones stand out giving an appearance of mongoloid facies. Expansion of the upper and lower maxillas may cause malposition of the teeth and malocclusion of the jaws. The roentgen changes in the skull are not necessarily proportional to those in the long bones.

In the long bones, the narrow cavity is widened, the cortex is thinned and atrophic, the spongiosa is deformed and partially destroyed, and the marrow cavity is crossed by irregular and distorted trabeculae, which may enclose cyst-like areas. Frequently there are heavy horizontal striations near the ends of the diaphyses of the long bones which are distinctly suggestive of irregular "growth lines." The bones are increased in diameter and the ends are more rectangular than usual, so that the lower ends of the femurs, for example, show an Erlenmeyer flask deformity, and the normally concave borders of the metacarpals become convex. Sometimes, the spongiosa is almost completely destroyed and the bones have a swollen, ground-glass appearance in contrast to the usual coarse trabeculated pattern. The appearance in such short bones as the metacarpals matches those in the flat bones. Exaggerated trabecular markings are found in the ilia and scapulas. The ribs are widened. The vertebral bodies are cupped; they are relatively shortened in vertical height and are widened.

Bone changes may be evident by the end of the first year of life. They are usually progressive in the growing child. However, in those individuals who live beyond adolescence, some irregular sclerosis is found, probably due to thromboses with infarction. There may be patchy cortical thickening, narrowing of the medullary cavity, loss of bone tissue and periosteal reaction.[36] Translucent areas ringed by sclerotic bone may be seen resembling the bone infarcts of caisson disease. In several cases, there is retardation of growth and infantilism.

The bone changes in sickle cell anemia are usually less marked than in Cooley's, but on occasion there is little difference between the two.

In sickle cell disease, the parietal bone is more likely to be involved than the frontal. The calvarium is increased in diameter and the tables are thinned. Because the disease appears symptomatically at a later age than Cooley's and because even the severely affected patients live much longer hemorrhage and fibrosis are more prominent. Bone infarction and patchy sclerosis is more often seen in the long bones and spine. Bone deformities such as kyphosis, scoliosis and saber shins are frequent as is oxycephaly.

In congenital hemolytic jaundice, bone lesions are still less frequent. However, a very few cases show bone lesions as extensive as in Cooley's anemia. Developmental anomalies, however, seem to be more common. Oxycephaly has been described by many authors. Less frequently, prominent eyes, epicanthus, an abnormally wide nasal root, persistence of deciduous teeth, absence of incisors, fanglike canines, polydactylism and brachydactyly have been observed. Growth may be impaired. It is significant that similar developmental anomalies have been described in other dystrophic disturbances such as hereditary non-spherocytic hemolytic anemia,[37] and erythroblastosis fetalis.[4] Bone decalcification on a familial basis has also been related to achylia gastrica of the pernicious anemia type.[38]

The alteration in bone structure in these diseases is so striking that one would anticipate a well-defined pathogenesis, but so far as I know, none has been described. The statement that the hyperplastic marrow is responsible tells little about how and why. The basic abnormality in these dystrophies apparently is in the erythrocyte. Recent studies suggest that in the abnormal-shaped red blood cells the hemoglobin molecule differs physically from the normal, and that the configuration of the molecule may be different for each of the diseases.[39] Studies on zinc concentration and carbonic anhydrase activity in the sickling phenomenon suggest a role of this enzyme, but other reports challenge these data.[3, 32, 40, 41] In thalassemia some have thought the essential lesion depends on defective porphyrin synthesis.[9] While these data cannot be applied immediately to the elucidation of the pathogenesis of the bone changes, it is evident that powerful and ubiquitous mechanisms are disturbed.

Attention is drawn to the possibility that the adrenocorticosteroids will provide a means of investigating the subject further. In a recent report[3] there is reference to two cases of acquired idiopathic hemolytic

jaundice which showed striking hematologic improvement under therapy. Treatment of a case of pernicious anemia suggested that ACTH favors release of preformed elements from the bone marrow and may increase the rate of maturation but is not capable of inducing bone marrow regeneration. A case of Cooley's anemia in a severe crisis was treated recently with ACTH by Dr. M. J. Whitelaw of Phoenix. There was a satisfactory clinical response but the patient also received transfusions and it is difficult to evaluate the contribution of the ACTH to the improvement. There has been no distinct hematologic improvement. At the end of four months, the therapy being continued, there has been no striking change in the bones but there is a suggestion of new bone formation in the diploe between the two tables of the calvarium and perhaps slightly sharper trabeculae in the long bones. It would be most interesting should a definite change in the bone become apparent, since it would then be likely that when adrenal hypercorticoidism is induced, the bone matrix is protected from the changes following defective erythropoiesis[33] and more normal bone is found in spite of the negative calcium balance.

Conclusions

I have reviewed what I consider to be the significant recent advances in the study of the skeletal lesions found in certain diseases of the blood. These new data suggest to me that, in the primary blood disorders, there is a change in the metabolic and enzyme systems, qualitatively and/or quantitatively specific for such disease, which alters the protein substrate available for bone formation and the physicochemical conditions for calcium precipitation. I suggest that the bone changes may, in certain cases, be a secondary tissue reaction based on these physicochemical alterations rather than a purely local cellular response to the adjacent disease process.*

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[REFERENCES ON NEXT PAGE]

REFERENCES

1. Anlyan, A. J., Gamble, J. and Hoster, H. A. Beta-glucuronidase activity of the white blood cells in human leukemias and Hodgkin's disease, *Cancer*, 1950, *3*:116.
2. Valentine, W. N., Pearce, M. L. and Lawrence, J. S. Studies on the histamine content of blood, with special reference to leukemia, leukemoid reactions and leukocytosis, *Blood*, 1950, *5*:623.
3. Vallee, B. L. and Altschule, M. D. "Trace" metals in blood with particular reference to zinc and carbonic anhydrase, *Blood*, 1949, *4*:398.
4. Caffey, J. P. *Pediatric X-ray diagnosis*. Chicago, Year Book Publishers, 1945.
5. Silverman, F. N. Skeletal lesions in leukemia, *Am. J. Roentgenol.*, 1948 *59*:819.
6. Dale, J. H., Jr. Leucemia in childhood, *J. Pediat.*, 1949, *34*:421.
7. Craver, L. F. and Copeland, M. M. Changes of bone in leukemia, *Arch. Surg.*, 1935, *30*:639.
8. Ewing, J. *Neoplastic diseases*. 3.ed. Philadelphia, Saunders, 1928.
9. Erb, I. H. Bone changes in leukæmia; pathology, *Arch. Dis. Childhood*, 1934, *9*:319.
10. Thomas, S. F. In discussion of paper by Harvey, R. M. on Wilms tumor, *Radiology*, 1950, *54*:699; and *Personal communication*.
11. Custer, R. P. *An atlas of the blood and bone marrow*. Philadelphia, Saunders, 1949.
12. Weber, E. J., Karpinski, E. E. and Heinle, R. W. Treatment of acute leucemias of childhood with folic acid antagonists, *J. Pediat.*, 1950, *36*:69.
13. Silverman, F. N. Treatment of leukemia and allied disorders with folic acid antagonists, *Radiology*, 1950, *54*:665.
14. Pearson, O. H., Eliel, L. P. and Talbot, T. R., Jr. Use of ACTH and cortisone in neoplastic diseases, *Bull. New York Acad. Med.*, 1950, *26*:235.
15. Karpinski, F. E. and Martin, J. M. Skeletal lesions of leukemic children treated with "aminopterin," *J. Pediat.*, 1950, *37*:208.
16. Farber, S. Some observations on the effect of folic acid antagonists on acute leukemia and other forms of incurable cancer, *Blood*, 1949, *4*:160.
17. Neuhauser, E. B. D. *Personal communication*.
18. Welch, A. D. et al. Folic acid-derived growth factor for *Leuconostoc citrovorum* in human urine, *Federation Proc.*, 1950, *9*:351.
    Broquist, H. P. et al. Some biological and chemical properties of the citovorum factor, *Ibid.*, 1950, *9*:18.
19. Haden, R. L., Bortz, D. W. and Portmann, U. V. Treatment of leukemia and polycythemia vera, in *Clinical therapeutic radiology* (Portman, U. V., ed.), New York, T. Nelson & Sons, 1950, p. 571.
20. Skipper, H. E., Riser, W. H., Jr. and Nolan, C. W. Specificity of 4-aminopteroylglutamic acid (aminopterin) for leukemic hematopoietic tissue, *Blood*, 1950, *5*:358.
21. Winzler, R. J. *M. Bull. Univ. Southern California*, 1950, *2*:18.
22. Stekol, J. A., Bennett, M. A., Weiss, K., Halpern, F. and Weiss, S. Sulfur-containing amino acids in growth with a labile methyl-free diet containing vitamin B_{12}, *Federation Proc.*, 1950, *9*:234.
23. Follis, R. H. *The pathology of nutritional disease*. Springfield, Ill., Thomas, 1948.
24. Hagtvet, J. Ascorbic acid in blood in health and disease, *Mat.-Naturv. Klasse*, 1945, no. 2:1; abstract in: *Chemical Abstracts*, 1947, *41*:796.
25. Snapper, I. *Medical clinics on bone diseases*, 2. ed. New York, Interscience Publishers, Inc., 1949.
26. Wintrobe, M. M. *Clinical hematology*. 2. ed. Philadelphia, Lea & Febiger, 1946.
27. Wyatt, J. P. and Sommers, S. C. Chronic marrow failure, myelosclerosis and extramedullary hematopoiesis, *Blood*, 1950, *5*:329.
28. Crail, H. W., Alt, H. L. and Nadler, W. H. Myelofibrosis associated with tuberculosis, *Blood*, 1948, *3*:1426.
29. Sussman, M. L. Myelosclerosis with

leukoerythroblastic anemia, *Am. J. Roentgenol.*, 1947, *57*:313.
30. Block, M. and Jacobson, L. D. Myeloid metaplasia, *J.A.M.A.*, 1950, *143*:1390.
31. Schwartz, S. O. and Ehrlich, L. The relationship of polycythemia vera to leukemia, *Acta haemat.*, 1950, *4*:129.
32. Thorn, G. W. et al. Clinical usefulness of ACTH and cortisone, *New England J. Med.*, 1950, *242*:783.
33. Ragan, C. et al. Effect of ACTH and cortisone on connective tissue, *Bull. New York Acad. Med.*, 1950, *26*:251.
34. Vaughan, J. M. Leuco-erythroblastic anæmia, *J. Path. & Bact.*, 1936, *42*:541.
35. Carpenter, G. Myelosclerosis. *Annual Rev. Med.* 1950, *1*:364.
36. Macht, S. H. and Roman, P W. Radiologic changes in sickle-cell anemia, *Radiology*, 1948, *51*:697.
37. Crosby, W. H. Hereditary nonspherocytic hemolytic anemia, *Blood*, 1950, *5*: 233.
38. Fiorentini, G. Paradenziopatia distrofica familiare progressiva, *Policlinico (sez prat.)*, 1947, *54*:853.
39. Ponder, E. Red cell shape and molecular arrangement of hemoglobin, *Blood*, 1950, *5*:293.
40. Mote, R. *Personal communication.*
41. Levin, W. C. and Schneider, R. G. Studies of the sickling phenomenon (abstract), *Am. J. Med.*, 1950, *9*:263.

VASCULAR COMPLICATIONS OF DIABETES MELLITUS*

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THE generally accepted definition of diabetes mellitus as an impairment of carbohydrate metabolism due to *insulin insufficiency* is inadequate. It should include the associated phenomenon of *premature vascular degeneration* as an integral part of the clinical syndrome.[1] The *diagnosis* of diabetes mellitus cannot be limited merely to a few classical symptoms fortified by *chemical* determinations of urine and blood sugar but must include *clinical* recognition of the generalized systemic manifestations of the disease.

A number of different procedures are responsible for the induction of diabetes both experimentally and clinically, through the production of relative or absolute insulin deficiency, e.g.:

1. An absolute decrease in available insulin (severe intrinsic pancreatic disease and total pancreatectomy).

2. Increased need for insulin due to its increased utilization (overfeeding, obesity and hyperthyroidism).

3. An increase in the rate of insulin destruction (infection and trauma).

4. A decrease in the responsiveness of the enzyme systems affected by insulin (endocrine factors such as purified growth hormone, crude anterior pituitary extract, adrenal cortical steroids, and ACTH, and liver disease).

5. The production of insulin antagonists or neutralizing agents.

The multiplicity of possible etiologic mechanisms justifies classification of diabetes mellitus as a symptom complex and not a specific disease entity except for the relatively infrequent instances of pancreatic desruction or extirpation and adrenal cortical hyperfunction.

Whatever etiologic factors finally result in the manifestation of hyperglycemia and glycosuria, they must be operative in the pathogenesis

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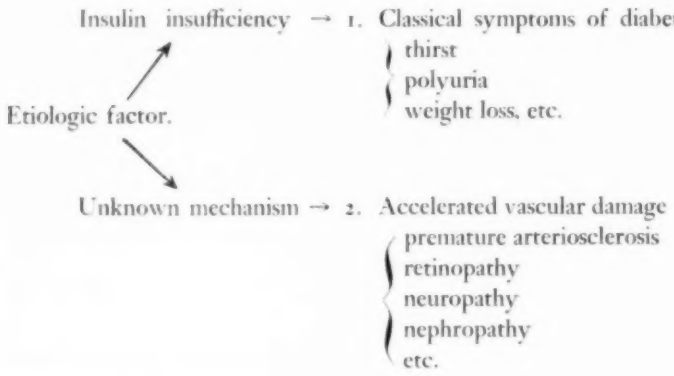
of diabetes *long before* a disturbance of carbohydrate metabolism becomes obvious. The bearing of an excessively large infant may portend the future onset of diabetes in the mother. So-called "diabetic complications" are often fully developed by the time glycosuria or the classical symptoms of thirst and polyuria are noted. Although this is generally true of patients beyond middle age, even young adults may present evidences of premature, accelerated vascular damage such as diabetic retinopathy, etc. without hyperglycemia and little or no impairment of glucose tolerance.[2] This is further substantiated by Colwell's[3] ingenious calculations that diabetes has progressed through half its course by the time clinical recognition is effected.

From the standpoint of dynamics, diabetes mellitus may be conceived as comprising two distinct groups of manifestations developing at different rates of speed.



Observation of totally depancreatized human beings over a period of the next twenty years will prove whether simple insufficiency of insulin alone can be responsible for the degenerative changes. In the average case of diabetes mellitus this relationship is obscured by possibility of degenerative or catabolic effects arising *independently* from as yet unknown etiologic factors. Arteriosclerosis, hypertension and diabetes mellitus may have a common origin, the causative agent producing insulin insufficiency only incidentally and only in susceptible individuals.

The primary appearance of typical "diabetic" symptoms which characterize the onset in all juvenile, most young adult and one third of the

VASCULAR DAMAGE IN TWO HUNDRED PATIENTS

Age of Onset of Diabetes	*No. of Patients*	*At the Time of Onset of Retinal Hemorrhage*				
		Average Duration of Diabetes, Yrs.	*Patients with Hypertension*		*Patients with Albuminuria*	
			No.	*%*	*No.*	*%*
0-19	55	13.0	27	49.1	24	43.6
20-29	21	13.3	9	42.9	10	47.6
30-39	45	13.0	21	46.7	23	51.1
40-49	79	10.0	37	46.8	48	60.8
Total	200		94		105	

older adult patients overshadows the insidious, slowly progressive secondary degenerative changes for a number of years. With *increasing duration* of diabetes, however, the latter break through the unrecognized subclinical stage finally to produce a variety of clinical manifestations, formerly regarded as "complications." An average of about thirteen years duration of diabetes has been noted as the time of the first appearance of these secondary associated phenomena.[1]

The disparity of primary and secondary manifestations at the *onset* and their fusion later in *young* diabetic patients may be depicted as follows:

	Onset	*13 to 20 years later*
Symptoms of Insulin Insufficiency	+	+
Accelerated Vascular Damage	0	+

The course of degeneration in juvenile diabetes varied widely, with no apparent relation to the amount of insulin required or to the ability to control glycosuria. Rapidly progressive lesions were noted in some young patients whose glycosuria was marked and almost constant as well as in some in whom glycosuria was rare and mild. Inexplicably, several juvenile diabetics, displaying persistent glycosuria, presented only minimal lesions of vascular damage by the twenty-fifth year. Their fate was no worse than that of the youngsters whose observance of diet and management with insulin afforded no difficulty in avoiding appreciable glycosuria. Some factor as yet unknown must be invoked to explain the

inherent resistance of the vascular systems of these two differently treated groups of young patients whose lesions progressed relatively slowly.

"The prognosis of diabetes in childhood—taking a long view—is in spite of the progress of dietary and insulin treatment more adverse than had originally been expected."[4] My observations revealed diabetic retinopathy in every instance within a twenty-five year duration of the disease.[1] This has now been confirmed by others.[5, 6] White,[5] in a survey of 200 juvenile patients surviving 20 years of diabetes, found vascular damage in 92 per cent, while Chute,[6] in a smaller group with similar duration, noted it in 85 per cent. The most dismal report, that of Fanconi's Clinic,[7] concludes that "16 years after the commencement of diabetes no patient is free from nephropathy; after 21 years not a single patient is still alive." A tour of the continent of Europe failed to reveal a single case entitled to a victory medal for having lived with diabetes for twenty-five years without evidences of vascular damage, according to Joslin.[8]

Classical "diabetic" symptoms *cannot* be elicited in *over fifty per cent* of middle aged and elderly patients when glycosuria is first discovered.[9] At this time many of the asymptomatic patients and about one-fifth of the group with "diabetic" symptoms already present evidences of accelerated vascular degeneration.[1] In fact, the degenerative phenomena may precede the appearance of hyperglycemia and glycosuria.

The three types of *onset* of diabetes in patients *beyond middle age* may be depicted in contrast with that of younger individuals, as follows:

	Onset		
Symptoms of Insulin Insufficiency	o	+	+
Accelerated Vascular Damage	+	+	o

Such differences in the clinical course account for the high incidence of unrecognized diabetes and the finding of a "casual onset" or an "onset with complications" in *66 per cent* of all patients.[9] Only *34 per cent* presented themselves because of "diabetic" symptoms.

The incidence of premature arteriosclerosis in the adult as measured by retinopathy, hypertension and albuminuria appears to be identical with that in the juvenile diabetic. Here, too, the earliest retinal lesions were noted about thirteen years after onset of diabetes, and associated with hypertension and albuminuria in about 50 per cent of patients.[1] An

apparent acceleration of the lesions was typical of the mild cases in this older age group, because of the insidious undramatic onset of diabetes so that duration of the disease could not be determined accurately. The incidence of fatal coronary disease in diabetes is *twice* that of non-diabetic males and *triple* that of non-diabetic females.[10] Therefore, suspicion of asymptomatic diabetes should be aroused in every case of *coronary artery disease*, particularly in *women* since they normally present an incidence of such cardiovascular involvement only about half as frequently as men. The diabetic predisposition to *peripheral vascular disease* is even more striking. Bell[11] claims that on the basis of arteriosclerosis alone, *gangrene* develops nearly *forty* times more frequently in diabetic than in non-diabetic individuals. As with coronary artery disease, diabetes obliterates the normal sex differences of masculine predominance in peripheral arteriosclerosis, the frequency in both sexes being equal when diabetes is present. Mirsky[12] noted a similar equalization of the sexes with respect to the incidence of diabetic neuropathy, impairment of vibratory sense perception appearing soon after the onset of diabetes and increasing strikingly after 13 years duration of the disease, the same period of time previously observed for the average onset of early retinopathy. As in retinal damage, the neurologic disturbances could not be correlated with the age of the patient, the "severity" of diabetes or the level of "control" of glycosuria.

Nerve tissue, which also includes the retina, represents the most sensitive indicator of vascular damage, with minute lesions often producing major disturbances. These degenerative manifestations are so varied and so protean in character that diabetes now surpasses syphilis as "the Great Imitator." Involvement of the nutrient vessels, the vasa nervosum, occurs in both central and peripheral portions of the nervous system. In addition to the well known diabetic "complications" of peripheral neuropathy increasing recognition is being given to similar vascular lesions of the brain stem, mid-brain, cerebrum, spinal cord and autonomic nervous system. The classic syndrome of occlusion of the posterior inferior cerebellar artery is characteristic of diabetes. Intramedullary hemorrhage accounts for the transient external ocular muscle paralysis which Weinstein and I[13] reported as being more frequently associated with diabetes than with lues. Pupillary abnormalities, including Argyll Robertson pupils, are also indicative of mesencephalic involvement on a diabetic vascular basis. Vascular myelopathy may lead to the development of

diabetic pseudotabes, Charcot arthropathy, impotence, neurogenic bladder and bowel disturbances, trophic skin changes and ulcerations, muscle atrophy due to anterior horn degeneration, etc. Disturbances in autonomic nerve supply plus the added insult of peripheral neuropathy jeopardize the diabetic patients already suffering from circulatory impairment of the extremities. Unfortunately the vascular lesions in both nerve and retinal tissue, being irreversible, do not respond to the administration of vitamin or protein supplements or to treatment of the underlying diabetic state itself. Therapeutic failure has followed the use in large doses of all the components of the vitamin B complex, including B_1 and B_{12} and the various preparations purporting to contain vitamin P, such as rutin and hesperidin.[14] In fact recent evidence indicates that none of the flavonoid substances including rutin are even absorbed in any appreciable amounts.[15]

Accelerated vascular damage which is an associated phenomenon and not a complication of diabetes appears to be related primarily to the duration of the disease; its course up to the present time has not been altered significantly by the use of insulin, the type of diet or the level of control of glycosuria and hyperglycemia. The subject of arteriosclerosis in diabetes mellitus has been limited to consideration of late complications such as gangrene, peripheral vascular and coronary artery disease. The existence of earlier generalized lesions is now generally recognized and the physician must broaden the scope of his examination of diabetic patients, searching persistently for evidences of incipient vascular damage. The usual analysis of urine and blood for glucose and the traditional catechism regarding the diet are inadequate for a complete evaluation of the patient's condition. Careful scrutiny of the fundi for early retinal hemorrhages, examination of the urine for albumin and casts, measurement of vibratory sense perception, and determination of the blood pressure on every visit with the diabetic patient will reveal an astonishing incidence of abnormalities in these areas. Thereby will be revealed a common paradox wherein the so-called "mild diabetic" patient may be found manifesting "severe complications," and conversely the so-called "severe diabetic" patient at times displaying only "mild vascular complications." However, regardless of the severity of the condition or its treatment, accelerated vascular damage is the inevitable fate of all patients suffering from diabetes mellitus at the present time.

[REFERENCES ON NEXT PAGE]

REFERENCES

1. Dolger, H. Clinical evaluation of vascular damage in diabetes mellitus, *J.A.M.A.*, 1947, *134*:1289.
2. Wagener, H. P. Retinopathy in diabetes mellitus, *Proc. Am. Diabetes A.*, 1945, *5*:203.
3. Colwell, A. R. Observed course of diabetes mellitus and inferences concerning its origin and progress, *Arch. Int. Med.*, 1942, *70*:523.
4. Rosenbusch, H. *Prognose und Spätkomplikationen des Diabetes Mellitus im Kindesalter*. Basel, S. Karger, 1945.
5. White, P. and Waskow, E. Arteriosclerosis in childhood diabetes, *Proc. Am. Diabetes A.*, 1948, *8*:139.
6. Chute, A. L. Survey of patients with juvenile diabetes mellitus, *Am. J. Dis. Child.*, 1948, *75*:1.
7. Fanconi, G., Botsztejn, A. and Kousmine, C. Die Nephropathie beim kindlichen Diabetes Mellitus *Helv. paediatrica Acta*, 1948, *3*:341.
8. Joslin, E. P. *Personal communication.*
9. Beaser, S. B. Clinical characteristics of early diabetes mellitus, *New England J. Med.*, 1948, *239*:765.
10. Clawson, B. J. and Bell, E. T. Incidence of fatal coronary disease in nondiabetic and in diabetic persons, *Arch. Path.*, 1949, *48*:105.
11. Bell, E. T. Incidence of gangrene of the extremities in nondiabetic and in diabetic persons. *Arch. Path.*, 1950, *49*: 469.
12. Mirsky, I. A. *Personal communication.*
13. Weinstein, E. A. and Dolger, H. External ocular muscle palsies occurring in diabetes mellitus, *Arch. Neurol. & Psychiat.*, 1948, *60*:597.
14. Dolger, H. Fundus oculi as an indicator of vascular damage in diabetes mellitus, *Arch. Ophth.*, 1947, *37*:695.
15. Clark, W. G. and MacKay, E. M. Absorption and excretion of rutin and related flavonoid substances, *J.A.M.A.*, 1950, *143*:1411.

THE DIABETIC AS A SURGICAL RISK*

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INTRODUCTION

DIABETES. The modern treatment of diabetes has all but eliminated the surgical diabetic's fundamental handicap, i.e., the diabetes itself. Many writers, including Collens and Boas,[1] McKim,[2] and Allen,[3] have stated that surgery is now as safe in the diabetic as in the non-diabetic providing, of course, that the diabetes is well controlled. Consequently surgery in these patients is much less hazardous now than in the pre-insulin era when inability to control their metabolic disease pre- and postoperatively often resulted in fatal diabetic coma. The operative mortality was high especially when infection was the primary surgical condition as in the case of carbuncles, lesions of the lower extremities and in the acute abdomen. On the other hand major elective surgery was also dangerous and was often avoided because of its high mortality and the too frequent incidence of serious secondary infection in the operative field or the incision. Without insulin it was difficult to prepare the patient adequately for surgery and instead he was starved preoperatively and sent to the operating room malnourished and with his glycogen reserves well depleted. The added stresses of the operation, i.e., trauma to tissues, fluid and blood loss, and perhaps poorly selected or prolonged anesthesia (Wilder[4]) further aggravated his metabolic imbalance. Finally in the postoperative period he often continued downward into possibly fatal acidosis since without insulin it was impossible to protect him by assuring adequate utilization of carbohydrate.

2. *Infection.* In more recent years the hazard of infection has been greatly reduced by the discovery of the sulfonamides and the antibiotics. To be sure the diabetic still reacts more poorly to infection than does the non-diabetic especially in relation to the skin, the lower extremities, and the urinary tract. However the aid of the new drugs in

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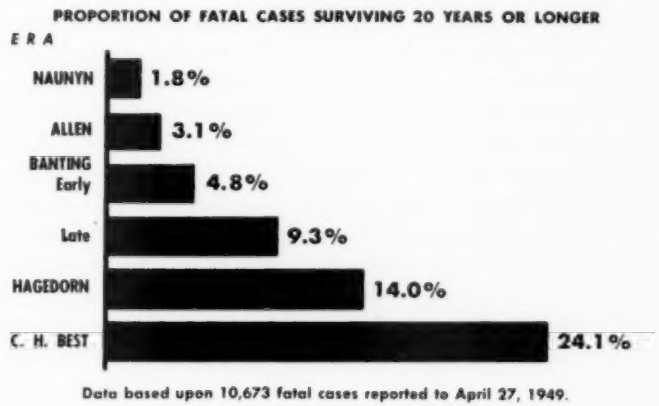
TABLE I—AVERAGE DURATION FROM ONSET TO DEATH IN SUCCESSIVE ERAS OF TREATMENT

Age at Onset (Years)	Years					
	Naunyn Era	*Allen Era*	*Banting Era*		*Hagedorn Era*	*C. H. Best Era*
	1897-1914	*1914-1922*	*1922-1929*	*1930-1936*	*1937-1943*	*1944-1949*
All Ages	4.9	6.1	8.0	10.4	12.5	14.4
Under 10	1.3	2.9	2.8	7.3	10.3	18.3
10-19	2.7	2.7	3.4	7.5	11.5	15.6
20-39	4.3	4.9	8.9	14.4	16.9	18.7
40-59	7.0	8.0	9.5	11.7	13.8	15.6
60 & over	4.4	6.4	5.5	7.1	8.8	9.4

From the George F. Baker Clinic (Joslin)

TABLE II



combatting infection has been of prime importance in making the diabetic a better surgical risk.

INCIDENCE OF SURGERY

As a result of the above advances in therapy assuring safer surgery in the diabetic, there has been a great increase in the incidence of surgery during the past twenty-five years. Joslin and Root[5] point out that whereas in 1923 there were only sixty-nine operations in diabetic patients

at the New England Deaconess Hospital, there were a total of 5004 (an average of 211 per year) from 1923 to 1946. They predict that "every other diabetic will need surgical treatment before he dies, and its success will be measurably affected by the degree of diabetic control attained during the preceding years." In the past four years (1946 to 1950) there has been a total of 1864 operations on Dr. Joslin's patients at the same hospital, an average of 466 per year.

At the same time, there has been a progressively increasing need for more surgery in the diabetics as their life expectancy has been extended by modern treatment. In a recent paper G. H. Pratt[6] reported that in 1948 there were ten times more diabetic admissions to large hospitals than in 1910, and concludes that the difference lay in the better modern medical management (i.e., with insulin, etc.) whereas in 1910 more diabetics died early of their disease or its complications. From data based on the experience of the George F. Baker Clinic, of which Dr. Joslin is the director, showing the duration of life from the onset of diabetes to death in successive eras of treatment, it is obvious that since diabetics are living longer more of them will require surgery. (See Table I). The same conclusion can be drawn from the data based on 10,673 fatal cases (same source) who survived twenty years or longer. (See Table II).

In addition to the fact that individual diabetics are living longer and requiring more surgery it is true that increasing numbers of diabetics are being added to the list as the life expectancy of the public as a whole is being gradually lengthened and more new diabetics are being discovered. The recent national diabetic detection drive indicates that there are approximately one million unknown diabetics among the population of one hundred and fifty million in this country. It is clear, therefore, that there is an ever increasing army of diabetics, a large proportion of whom must eventually require surgical treatment.

Arteriosclerosis

In evaluating the diabetic as a surgical risk we must consider in addition to the diabetes itself and the related problem of infection, the increased incidence of degenerative vascular disease in the diabetic. Widespread arteriosclerosis is characteristic of the elderly diabetic and because of its involvement of the vessels of the brain, heart, kidneys and lower extremities, is responsible for the most serious postoperative complications in these patients. The arteriosclerotic process also occurs

TABLE III—202 CASES WITH ONSET OF DIABETES BETWEEN AGES 15 AND 30

Duration (Years)	*0-10*	*11-20*	*21-29*
High Blood Pressure	2%	21%	33%
Calcified Arteries	21%	66%	88%
High Capillary Fragility	14%	57%	67%
Retinitis	4%	56%	60%
Proteinuria	3%	13%	10%
Average Age (Years)	28	39	47

From the George F. Baker Clinic (Joslin)

in the young diabetic, appearing prematurely and becoming progressively more extensive in proportion to the duration of the diabetes when the latter is uncontrolled. Joslin and White[7] report a series of 249 cases with fifteen to twenty years duration of diabetes and an average age of twelve years at onset. Significant complications were: (a) Arteriosclerosis in 106 of 154 cases examined or 70 per cent, (b) Retinal hemorrhage in 51 of 79 cases or 65 per cent, (c) Hypertension in 49 of 128 cases or 40 per cent, and (d) Albuminuria in 46 of 138 cases or 35 per cent. In another series of 202 cases from the experience of the George F. Baker Clinic, vascular complications in patients with the onset of diabetes between the ages of fifteen and thirty years show a progressive increase in proportion to the duration of the diabetes. (See Table III). It is evident from this data that young patients with diabetes of short duration are better surgical risks because of less vascular disease and, by the same token, the longer they live the more extensive their vascular disease and the poorer surgical risks they become.

SURGICAL MORTALITY

1. *General.* The improvement in diabetic surgical mortality continues due, in a large part, as stated above, to better control of the diabetes and of infection. It is true, however, that the modern care of the surgical patient (diabetic or not) has also been a factor. As pointed out by McKittrick[8] and others: (a) a better understanding of fluid balance and the use of parenteral feeding including vitamins and whole blood, (b) intestinal antiseptics in preparation for bowel surgery, (c)

TABLE IV—6868 DIABETIC OPERATIONS JAN. 1923 TO JAN. 1950
NEW ENGLAND DEACONESS HOSPITAL

	1923-1941	*1942-1946*	*1946-1950*
Amputations (Maj.)	733	269	216
Amputations (Min.)	450	322	417
Carbuncles	116	18	9
Ulcers, Abscesses	431	108	115
Thyroid	243	66	61
Tonsils	186	48	36
Laparotomy	428	132	286
Genito-Urinary	151	46	88
Pelvi-Rectal	234	56	167
Ocular	148	49	83
Miscellaneous	431	399	386
TOTALS	3551	1453	1864
Fatal Cases	260	32	37
Per cent Fatal	7.3	2.2	1.9

improved anesthesia, and (d) early mobilization, are all important in the successful surgical care of the diabetic.

Joslin[5] reports a steady fall in the overall operative mortality in his diabetics as follows: 1923 to 1926, mortality 11.5 per cent; 1923 to 1941 (3551 operations) mortality 7.3 per cent; 1939 (264 operations) mortality 6.4 per cent; 1942 to 1946 (1453 operations) mortality 2.2 per cent. The most recent tabulation, i.e., January 1946 to January 1950 shows a total of 1864 operations with an overall mortality of 1.9 per cent. (See Table IV). Sprague and Wilder[9] reported an earlier series of 260 operations from 1930 to 1939 (before the antibiotics) with a mortality of 4.3 per cent.

2. *Infection and Mortality*. A comparison of the mortality figures in the periods before and after the chemotherapeutic drugs and the antibiotics is especially striking in patients with gangrene and infection of the lower extremities. In McKittrick's[10] first series (1923 to 1928) the major amputation mortality was 16.1 per cent, nine out of fourteen fatalities being directly due to infection. This was reduced somewhat as experience with insulin increased and as the surgical treatment was improved and standardized. The series from 1923 to 1941 showed a major amputation mortality of 14.1 per cent with infection still playing

TABLE V—23 MAJOR AMPUTATION DEATHS (1942 TO 1950)

Cause of Death	*Cases*
Septicemia (Gas Bac.)	1
Coronary Occlusion	9
Cerebral Accident	2
Uremia	3
Bronchopneumonia	2
Pulmonary Embolus	4
Cause Unknown	2
Total Deaths	23
Summary—Infection	1
Vascular Disease	14
Other Causes	8

a major role. Finally, from January 1942 to January 1950 in which first the sulfonamides and then the antibiotics came into common use, the mortality suddenly dropped to 5.8 per cent. During that period there were 390 major amputations with twenty-three deaths. At the same time there were 733 minor amputations (including 272 transmetatarsals) with three deaths, *none due to infection*, a minor amputation mortality of 0.4 per cent. The combined major and minor mortality was 2.3 per cent.

3. *Arteriosclerosis and Mortality*. An analysis of the 23 deaths above in the major amputation group shows that *only one died of infection* (a gas bacillus stump infection and septicemia) while almost *two-thirds of the deaths* (i.e., 14) *were due to complications secondary to their vascular disease*. (See Table V). There were nine deaths from coronary thrombosis, two from cerebral thrombosis or embolus, and three from uremia. The other deaths were two from bronchopneumonia, two with cause undetermined and four from pulmonary embolus. Of the latter, two were definite but the other two were not proven. The above figures indicate that if infection is controlled in this group of diabetics the surgical risk is largely that of their cardiovascular disease.

4. *Other Factors in Mortality*. Other factors of importance which have reduced the operative risk and improved the results in this group of diabetics such as correct evaluation of local lesions, their pre-operative

management, indications for major and minor amputations, etc., cannot be discussed here. It should be stated, however, that the transmetatarsal amputation has been of great value in reducing the incidence of major amputation and has, therefore, been instrumental in reducing the overall mortality. L. S. McKittrick, J. B. McKittrick and T. S. Risley[11] have reported in detail on 215 cases done from 1944 to 1949 with two deaths. In the following year (1949) an additional 55 have been done with no deaths. Many of these patients would have required major amputation before the antibiotic era and with associated higher mortality.

Common Infections in the Diabetic

In some infections other than those of the lower extremities surgery has become unnecessary or much less frequent than formerly with the ability to control infection by the use of antibiotics. In others such is not the case.

1. *Carbuncles.* The large carbuncles formerly so serious in the diabetic have become a comparative rarity in hospital practice. There has not been a carbuncle death among the Joslin diabetics in the past six years, whereas in the previous three years (before the antibiotics) there had been three.

2. *Cellulitis.* Other infections such as lymphangitis and cellulitis can now be controlled and localized although surgical drainage is still indicated for frank collections of pus.

3. *Hand Infections.* Because of early and successful antibiotic therapy we no longer see the extensive hand infections that formerly required surgery including amputation of fingers or of the hand itself.

4. *Urinary Tract Infection.* Formerly, serious urinary tract infections occurred more frequently in the diabetic and were a difficult problem in management. They responded poorly to the then current urological treatment, recurrence was common, serious chronic infection often occurred and too many resulted in a fatal outcome. These infections were not only of the retrograde type resulting in pyelonephritis, but many were of hematogenous origin and were seen in patients who had furuncles, carbuncles, foot infections and septicemia. Perinephritic abscess was not an uncommon complication in these cases. Now, with chemotherapy and the antibiotics to control urinary tract infections early, serious retrograde extension can be prevented. Also by early treatment of the foci of infection mentioned above we can now elimi-

nate the possibility of blood-borne infection. In cases requiring operation for or with associated genito-urinary tract infection the new drugs, by giving added protection, have helped to reduce the surgical risk.

5. *Biliary Tract and Liver Infection.* Infection in relation to the extra-hepatic biliary tract almost always associated with gall stones is particularly dangerous to the diabetic not only because of the hazard of necrosis and perforation of an acute gall bladder but also because of the frequency of common duct obstruction with ascending infection and cholangeitis. This, of course, may produce further damage to the liver which, in the diabetic, already may be handicapped by pathological changes and disturbed liver function. The antibiotics have not been the answer to this problem but the teaching that cholecystectomy should be done as early as possible in controlled diabetics with gall stones (with or without symptoms), should do much to protect against this dangerous situation. Obviously the surgical risk is much greater in these patients if operation is postponed until they develop acute cholecystitis, jaundice, cholangeitis or pancreatitis.

During the four years ending January 1, 1946, cholecystectomy (with or without choledochostomy) was done on 39 Joslin diabetics without a fatality (Joslin and Root[5]), while in the last four years ending January 1, 1950, there were 49 cases with one death. The low mortality and successful results in these 88 cases indicate that gall bladder surgery is well tolerated by the controlled diabetic and is not associated with undue risk.

6. *Intra-abdominal Infection.* In intra-abdominal infection from any cause, most commonly appendicitis, the antibiotics now available cannot be depended upon and are indicated only as an adjunct to surgery. Early diagnosis and operation are essential in any acute abdomen. Diagnosis may be difficult in the diabetic for two reasons, first, the signs and symptoms may not be clear cut, and second, they may be similar to those associated with acidosis. To further complicate the picture both conditions, i.e., an acute abdomen and acidosis, may be present, the latter being secondary to the former. This problem in differential diagnosis cannot be discussed here in detail except to point out that if a diabetic with acidosis has abdominal signs and symptoms suggesting an acute abdomen which persist after the acidosis has been corrected by treatment, surgery is indicated. Under the above circumstances the delay of a few hours for treatment of the acidosis is justifiable.

Prophylactic appendectomy is indicated especially in the younger diabetics who have a history suggesting previous attacks of appendicitis. This not only eliminates the appendix as a source of future trouble but also simplifies evaluation of the abdomen if the patient is seen later in acidosis.

Specific Antibiotic Treatment

It should be pointed out that the general problem of infection control in the diabetic may not always be a simple one. Infection in any location may be due to an organism which proves to be resistant to a routine form of antibiotic therapy. This is especially true in a certain number of patients with foot lesions where the infection is a mixed one (streptococcus, staphylococcus and colon bacillus being the common organisms) which may not be sensitive to penicillin. It is important, therefore, that a culture be taken early and that sensitivity tests be done by the bacteriologist to determine which of the available antibiotics (i.e., penicillin, streptomycin, aureomycin and others) is most effective in inhibiting the growth of the patient's infecting organisms. By so doing valuable time will not be lost in trying ineffective antibiotic therapy over a period of days. A workable plan is to culture the lesion on admission, sending the culture to the laboratory with a request for sensitivity tests, and at the same time starting the patient on one of the penicillin preparations. A report on the tests can be obtained in twelve to twenty-four hours at which time the treatment can be changed to a more effective antibiotic if so indicated by the tests. The same method should be used in all infections whenever it is possible to obtain a culture. This has proven to be an important requisite for the successful management of infection in the diabetic.

Evaluation and General Management of the Surgical Diabetic

It is agreed by all who have had experience with the surgical diabetic that successful management and consequently a lower surgical risk depends upon close coöperation between the physician and the surgeon together with good, constantly available, laboratory facilities. To these essentials might be added an experienced and efficient hospital group of residents and nurses. The surgical diabetic requires frequent and combined medical and surgical observation, around-the-clock laboratory tests in many cases, and the best possible nursing care if he is to make

an uncomplicated recovery. Lack of coöperation or poor functioning of any of the above may seriously interfere with his recovery.

Proper evaluation and treatment of the surgical diabetic is essential. More specific considerations directed toward this end are as follows:

1. *The surgical disease itself* must be promptly evaluated both as to diagnosis and degree of urgency of operation. The latter decision must be that of the surgeon and based on fundamental surgical principles. If an acute abdomen or undrained sepsis demands emergency operation it should be done in spite of a high blood sugar or sugar in the urine. Prolonged delay while attempting to control the diabetes completely may be fatal and is never justifiable under any circumstances. Acidosis, however, seriously increases the surgical risk and if operation can be safely postponed for a few hours, the acidosis can often be corrected in that time. If such a delay is out of the question the increased risk of immediate operation in the presence of acidosis must be accepted and every effort made postoperatively to correct it.

2. *Evaluation and treatment of the patient's condition in general* (apart from the diabetes) is important and includes consideration of: (a) Age, (b) Mental and neurological status, (c) Nutritional state, (d) Hydration of tissues and fluid balance, (e) The blood in regard to cells, hemoglobin, electrolytes, colloids, etc., (f) Type, location and extent of infection, if present, (g) Respiratory status, and (h) Cardiorenal and general vascular status.

Having carefully evaluated the patient both medically and surgically, as outlined above, every attempt must be made to correct his physiological and organic difficulties (as well as his diabetes) before surgery is done. Obviously all diabetics do not require extensive studies preoperatively, particularly those with diabetes of short duration who have been well controlled and who have little or no vascular disease or other complications. Nor is it possible or advisable to carry out any but the essential pre-operative studies in emergency cases. However, even in the latter, dehydration and a disturbed electrolyte balance can be helped by parenteral fluids, anemia can be corrected by transfusion, and impaired cardiac function improved by supportive treatment. When time permits, infection, including that of the urinary tract can be reduced or controlled by chemotherapy and the antibiotics. The control of infection in general and in particular in the foot lesions has been discussed above. In the latter, emergency surgery is rarely indicated.

Correct evaluation of the blood supply of the extremities and control of the infection by the use of the appropriate and effective antibiotic together with diabetic control and the above general supportive measures are all essential in making the patient as good a surgical risk as possible.

3. *Management of the Diabetes.* It is beyond the scope of this paper to consider this problem in detail nor is it necessary to demand any specific plan of diabetic management. The fundamental principles of modern treatment are followed in all successful plans which, therefore, differ only in minor details. It would seem appropriate, however, to outline briefly the method used by the Joslin group at the New England Deaconess Hospital as reported several times by Joslin[5] and by McKittrick and Root.[12]

A. *Pre-operative preparation.* It should be the aim of the physician in preparing the diabetic for an operation of election to send him to surgery well fed, with the liver well stocked with glycogen and with the urine acid-free and showing little or no sugar. In well controlled cases no special preparation is necessary, therefore, other than an adequate diet with or without insulin. In these cases one to two days of pre-operative hospitalization is sufficient. Fluid intake should be adequate enough to produce a urinary output of 1000 to 1500 cc. daily. If necessary, intravenous normal saline (1500 cc.) with 5 per cent glucose is given and almost always is administered immediately before major surgery to insure adequate fluid and carbohydrate. No fluids are given by mouth for eight to twelve hours pre-operatively. In the untreated or uncontrolled diabetic longer pre-operative treatment is necessary before an elective operation to obtain sufficient nourishment and a good metabolic balance. Sudden restriction of carbohydrate is to be avoided in severe or elderly diabetics since it may result in acidosis, further disturbance in liver function or even anuria. Food should be fairly simple so as to avoid upsetting the stomach, which would make it difficult to continue with a well balanced full diet so necessary in preparation for surgery. Pre- and postoperative insulin administration is discussed under C below.

Over medication must be avoided especially in the elderly diabetic who is easily depressed by drugs. Too much pre-operative medication with the additional burden of anesthesia can result in serious central nervous system depression which may lead to secondary pulmonary or cardiovascular complications.

B. *Postoperative fluids and diet.* Adequate postoperative fluid intake is essential and as in the pre-operative patient should be sufficient to maintain a good urinary output. Most patients receive 1500 cc. of 5 per cent glucose in saline intravenously on return from the operating room. If adequate amounts of fluid cannot be taken or retained during the day this may be repeated later using distilled water rather than saline unless there is a chloride deficiency due to vomiting or other causes. In older patients with cardiac disease it is dangerous to give parenteral fluids too rapidly or in too large amounts.

Unless the operation requires otherwise the following dietary regime is used in most general surgical cases. On the first postoperative day clear liquids such as water, gruel made with water, tea and coffee are given freely. Dilute fruit juices may be used but sparingly. On the second postoperative day fluids with milk are added together with ice-cream, cooked cereals, and custard if desired. On the third day and thereafter the diet is gradually increased as tolerated. It is necessary that the patient get at least 150 grams of carbohydrate daily throughout the postoperative period. If this cannot be taken by mouth it is supplied by parenteral administration. At discharge many patients have reached a diet of approximating 160 grams of carbohydrate, 75 grams of protein and 90 grams of fat. The diet after operation should contain as a minimum between 0.66 and 1.25 grams of protein per kilogram of body weight.

C. *Insulin management.* If insulin has been used regularly by the patient the same total number of units usually given in twenty-four hours is continued daily in most postoperative patients. In the morning before operation the full dose of protamine zinc insulin is given or occasionally only one-half to two-thirds of it if the operation is scheduled for late in the morning. In many cases intravenous saline and glucose is given pre-operatively. One-half to the full dose of the patient's crystalline insulin is given on return from the operating room when an intravenous of 1000 to 1500 cc. of 5 per cent glucose in saline (or distilled water) is started. Late in the afternoon, several hours after the intravenous has run in, a blood sugar may be taken and more crystalline insulin given if indicated. If more fluid and glucose are desirable later on, more crystalline insulin is used to insure utilization of the carbohydrate. Great care is taken to avoid hypoglycemia because of the serious complications that may attend it.

The hospital group taking care of these patients must be on the alert for any signs of hyperinsulinism so that it can be corrected immediately by intravenous glucose. It is much safer to have some elevation of blood sugar and mild glycosuria in the postoperative diabetic, especially in those with much cardiovascular disease, than to overtreat with insulin and risk the possibility of fatal insulin reactions. As pointed out by McKittrick and Root[12] it is dangerous to attempt to cover all of the glucose given by parenteral means by insulin. It must also be remembered that after drainage of infection the diabetic will require less insulin than before. The hazard of giving insulin on the basis of sugar in the urine following intravenous glucose or on the basis of urine sugar in patients with urinary retention is well known.

If the patient is one in whom insulin has not been used before, it is given when two successive specimens contain sugar and omitted when two successive specimens are sugar-free. In these cases small doses every three to four hours are safer than large doses infrequently until the tolerance of the patient has been determined. During convalescence when the urine is sugar-free, the need for insulin is tested by reducing the noon dose first and then the evening dose. Blood sugar determinations as a guide to insulin administration should be taken in the late afternoon as well as before breakfast.

It is not necessary to further emphasize the importance of good diabetic control in the surgical diabetic both before and after operation. To quote E. R. Snader, Jr.[13]: "Surgical cases sometimes die with diabetes but should not die of diabetes, if properly managed by a competent internist." Control is not only important in relation to surgical risk but also in healing of the operative site and the incision. It is true (Wilder[1]) that in the well controlled diabetic healing occurs just as rapidly and as well as in the non-diabetic.

Anesthesia

Proper selection and administration of the anesthesia are of great importance in diabetic surgery not only from the point of view of its effectiveness during the operation but also in respect to the patient's well-being both on the table and after his return from surgery. The choice of anesthesia must be based primarily on the surgical indications but one must also consider the diabetic's reaction to the various anesthetic agents and select the one that is most satisfactory surgically and at the

same time least hazardous to the patient. In any case the diabetic in general stands anesthesia poorly and therefore the duration should be as short as possible (as should the operation) and if a general anesthesia is being used the avoidance of anoxia is of the utmost importance. In this connection morphine and the barbiturates also tend to produce anoxia and if given pre-operatively the dose should be small. Excessive pre-operative medication in the elderly diabetic is discussed above.

In general, the anesthetics in the order of their safety in the diabetic are: 1. Local and regional. 2. Low spinal. 3. General. More specifically the various anesthetics in relation to the diabetic are as follows:

Local or regional. When the surgery permits, local or regional anesthesia is as satisfactory as in the non-diabetic but should never be used for operations on the lower extremities where there may be arterial deficiency. If used in the hand, it should be only in the simplest procedures using the same precautions as in the non-diabetic, i.e., never add adrenalin to the anesthetic in doing a digital nerve block or when using a finger tourniquet.

Spinal. Spinal anesthesia is used almost exclusively in major and minor amputations at the New England Deaconess Hospital and has proven most satisfactory over a period of many years. Procaine or pontocaine is used in small doses so as to obtain a low level of anesthesia of short duration. It has also been satisfactory and safe in other surgery including laparotomy in young diabetics without extensive cardiovascular disease. It must be administered, however, by a skilled anesthetist who can control the level so as to avoid dangerous variations in blood pressure. It is contraindicated for abdominal surgery in elderly diabetics with extensive cardiovascular disease or with hypertension in whom even a comparatively slight drop in blood pressure might be serious.

Refrigeration anesthesia. We have had no experience with this method and no occasion to use it since spinal has been so satisfactory in the amputation cases.

Cyclopropane. This anesthetic is satisfactory in the diabetic for short surgical procedures where full relaxation is not desired. It has a less deleterious effect on the diabetic than ether and less postoperative vomiting. It is used, however, primarily as an induction agent rather than a basic anesthetic since it is not easy to maintain satisfactorily for any length of time. Formerly it was used for induction before ether by the

Lahey Clinic in the Joslin diabetic thyroid cases. As with all general anesthetics used in the diabetic anoxia must be guarded against.

Ethylene. This anesthetic has been used very little in the surgical diabetic at the New England Deaconess Hospital in recent years. It produces less hyperglycemia than ether but, of course, much less relaxation. It is not suitable for prolonged anesthesia and a serious disadvantage is its inflammability when too diluted by air. Strict precautions must be taken against explosion if this anesthesia is used.

Nitrous Oxide-Oxygen. This anesthetic is not satisfactory for use in the diabetic except for very short operations or for induction before ether. Its disadvantages are, first, that it may be difficult to prevent anoxia and, second, muscle relaxation cannot be obtained without overdosage. It does, however, have less tendency to produce acidosis and there is a minimum of vomiting following its administration.

Ether. Acidosis of varying degrees is produced in the diabetic by ether anesthesia. The postoperative nausea and vomiting often associated with its use tend to interfere with an adequate intake of fluid and nourishment and therefore complicate the diabetic management. However, in operations in which relaxation is necessary or where local regional and spinal or the gaseous anesthetics cannot be used, ether is the only choice. It must be administered well and sufficient oxygen supplied with it. Fortunately its effects on the diabetes can be overcome in the postoperative period by careful treatment of the acidosis with insulin and by giving adequate amounts of parenteral fluids and carbohydrate until the diabetes is again under control.

Sodium Pentothal. This intravenous anesthetic is useful and safe for short procedures not requiring full relaxation. It is used a great deal for incision and drainage of abscesses and other simple operations. It has little effect under these circumstances on the diabetes. It is contraindicated in the elderly, very feeble patients, in those with severe liver disease, and when there is respiratory difficulty. Excessive pre-medications should be avoided and during the administration a free airway must be maintained. Oxygen should be available for use if necessary.

Bed Care of the Surgical Diabetic

The importance of constant alertness of doctors and nurses caring for surgical diabetics has been emphasized above. Early recognition and treatment of postoperative complications, no matter how minor, is

essential to successful recovery. Good nursing care is also necessary, not only in hastening recovery, but also in the prevention of complications. Diabetics are particularly susceptible to pressure lesions of the back and lower extremities and to skin irritation with secondary infection. These lesions are precipitated by inadequate nursing care. Therefore these patients must be turned frequently and every effort made to give them good skin care. Change of position together with supervision of deep breathing and leg exercises is also of value as prophylaxis against pulmonary complications and peripheral venous stasis. In this connection early ambulation, when possible, is as desirable as in the non-diabetic. Other essentials of good bedside nursing such as helping to insure adequate fluid and food intake, understanding of the patient's needs as far as comfort and reassurance are concerned, careful recording of valuable data such as urinary output, and quickness to recognize and report any abnormalities, are all important duties of the nursing staff.

Summary and Conclusions

1. There is a proportionately increased need for safe diabetic surgery as diabetics live longer and increase in numbers.

2. The control of diabetes and infection have been the essential factors in reducing surgical risk and mortality. Advances in surgery, anesthesia and understanding of the physiological needs of the surgical patient in general have also been important.

3. The diabetics' complicating vascular disease is now the chief hazard to surgery.

4. Close coöperation between physician and surgeon, and all concerned in the care of the surgical diabetic is essential.

5. Careful evaluation and good pre-operative preparation of the patient is necessary if surgery is to be successful. The surgical disease, the general medical status and the diabetes must be considered and handled promptly and efficiently. Correct postoperative management is equally important.

6. Adequate diabetic management with diet and insulin is of prime importance. Sufficient fluid and nourishment with enough insulin to insure adequate carbohydrate utilization is necessary both pre- and postoperatively. Hypoglycemia is dangerous especially to the elderly patients or those with extensive cardiovascular disease, and must be avoided.

7. Emergency surgery must not be delayed while attempting to control the diabetes completely. A short delay is justifiable, however, for treatment of acidosis. The latter increases the operative risk and should be eliminated if possible.

8. Early control of infection, regardless of site, is important in the diabetic. This is best obtained by the prompt use of the most effective antibiotic as determined by bacteriological sensitivity tests.

9. Prophylactic cholecystectomy is advisable in diabetics with gall stones (with or without symptoms) whose condition permits, and when good facilities for care are available. Prophylactic appendectomy is also logical and desirable especially in younger diabetics who have had symptoms suggestive of appendicitis.

10. Good anesthesia is an essential factor in surgical risk. The anesthetic chosen should be one that is not only surgically satisfactory but also safest for the patient. If a general anesthetic is used its duration should be as short as possible and every effort made to avoid anoxia.

11. The diabetic, if correctly evaluated and well managed medically and surgically, is as good a surgical risk as the non-diabetic with a comparable amount of general vascular disease.

REFERENCES

1. Collens, W. S. and Boas, L. C. *The modern treatment of diabetes mellitus.* Springfield, Ill., Thomas, 1946, chap. 24.
2. McKim, L. H. and Fowler, A. F. Surgery in diabetes mellitus. *S. Clin. North America.*, 1945, *25*:1027.
3. Allen, F. N. Treatment of diabetes in relation to surgical operations, *S. Clin. North America*, 1943, *23*:830.
4. Wilder, R. M. *Clinical diabetes mellitus and hyperinsulinism.* Philadelphia, W. B. Saunders Co. 1940, chapt. 12.
5. Joslin, E. P., Root, H. F. et al. *Treatment of diabetes mellitus.* 8 ed. Philadelphia, Lea and Febiger, 1946, chapt. 26.
6. Pratt, G. H. Surgical management of diabetes; including amputations, *Bull. New York Acad. Med.*, 1948, *24*:111.
7. Joslin, E. P., Root, H. F., White, P. et al. *Treatment of diabetes mellitus.* 8 ed. Philadelphia, Lea and Febiger, 1946, chapt. 28.
8. McKittrick, L. S. Recent advances in the care of surgical complications of diabetes mellitus, *New England J. Med.*, 1946, *235*:929.
9. Sprague, R. G. and Wilder, R. M. The management of the surgical diabetic patient, in *Textbook of surgery*, edited by Frederick Christopher, 3 ed. Philadelphia, Saunders, 1942, p. 1685.
10. McKittrick, L. S. and Root, H. F. *Diabetic surgery*, Philadelphia, Lea and Febiger, 1928.
11. McKittrick, L. S., McKittrick, J. B. and Risley, T. S. Transmetatarsal amputation for infection or gangrene in the diabetic, *Ann. Surg.*, 1949, *130*:826.
12. McKittrick, L. S. and Root, H. F. Preoperative and postoperative treatment of the patient with diabetes, *Arch. Surg.*, 1940, *40*:1057.
13. Snader, E. R., Jr. Notes on diabetic patient as a surgical risk, *Hahneman. Monthly*, 1949, *81*:399.

DEDICATION—BLOOD TRANSFUSION ASSOCIATION BUILDING*

BENJAMIN P. WATSON

President, The New York Academy of Medicine

WE are met here this afternoon to inaugurate and dedicate this new home of the Blood Transfusion Association and in doing so to congratulate the Association upon the splendid work it has done in the past, and to wish for it continuing and enlarging usefulness in the future.

An occasion such as this has real meaning only insofar as it affords an opportunity to dedicate ourselves to that future and to seek inspiration and stimulus from the example of those who conceived the idea of such an organization and who through the years of its growth and development have carried on its day-to-day activities.

As with every other advance in medicine, the present status of blood transfusion as a therapeutic measure has been achieved as the result of a gradual evolution and by the application to its practical use of discoveries in various branches of biological science.

As early as the 17th century there are records of the transfusion of the blood from lower animals to man, a few of them fortuitously successful or at least not fatal to the recipient. Later, with the invention of the syringe, it became possible to transfer blood from human to human but these early attempts were fatal in 50 per cent of the cases because of the introduction of sepsis and, as we now know, of incompatibility of the bloods. So the method fell into disrepute.

At the beginning of this century it was realized that some patients who had suffered severe loss of blood could be saved if blood volume were restored by the infusion of normal saline solution and this became a recognized procedure. The drawback to it was that the fluid soon left the circulation and diffused into the tissues so the procedure might have to be repeated several times within a short interval. A solution which would not so diffuse was sought for and was found in gum acacia. This

* Address delivered at the dedication ceremonies of the Blood Transfusion Association on the occasion of the 21st Anniversary of its establishment held on June 7, 1950 in the new building of the Association at 178 West 102nd Street, New York 25, N. Y.

solution remained longer in the circulation but its use was often attended by very unpleasant and sometimes fatal reactions. It did, however, save many lives as I can personally attest from my experience in the first World War.

With the perfecting of aseptic and operative techniques it then became possible to perform direct transfusion of blood from donor to recipient by hitching up an artery of the former to the vein of the latter. I first saw this done by the late Dr. Crile in Cleveland in the year 1913. Then came the syringe method in which with syringes specially prepared to prevent clotting, the blood was drawn from the vein of the donor and immediately injected into that of the recipient as they lay side by side in the operating room. This was the method in most general use when I came here in 1926.

Much earlier than this, however, in 1914, Agote in Buenos Aires and others had demonstrated that by adding sodium citrate to the blood, coagulation was prevented and so the blood could be collected from the donor and later transfused to the recipient. The blood could be stored and called for as required—the actual presence of the donor at the time of the transfusion was no longer necessary. Thus the idea of a blood bank became a possibility and later an actuality.

Up to the year 1901 it had been believed that the blood of each species in the animal world was uniform. In that year Karl Landsteiner made the discovery that there were four types of human blood and that agglutination of the red cells would result if one were mixed with another. He pointed out the importance of this observation in blood transfusions but little practical attention was given to it for some years. During these years, in spite of the gradual perfecting of the mechanical techniques of transfusion, undesirable and sometimes fatal reactions occurred. Donors were still being recruited in a very haphazard manner.

It was at this stage when the therapeutic value of blood transfusions, not only in cases of blood loss but in various other pathological states was fully recognized, but its performance attended with difficulties and dangers, that the Blood Transfusion Betterment Association came into being. The title indicated its purpose. In 1941 the "betterment" having been accomplished, its title was changed to the present one, the Blood Transfusion Association.

The prime mover in bringing about the organization was The New York Academy of Medicine. The circumstances were these.

In 1927 the Committee on Public Health Relations of the Academy urged upon the Department of Health the maintenance of strict supervision over blood donors and the commercial agencies through which they were obtained. It continued to advise the health authorities on the type of regulations which should be adopted until in 1930 Section 109 of the Sanitary Code was enacted.

In 1929, Dr. John A. Hartwell was President of the Academy and he was also associated with Cornell University Medical College and New York Hospital where Dr. Arthur F. Coca, then Professor of Immunology at the school and an associate in the hospital laboratory, originated the idea of a cooperative blood donor agency. The situation at that time was most unsatisfactory. Donors were collected by enterprising individuals from among Bowery tramps and others of that type. They were inadequately examined and bled white. No one cared, and the surgeons were at their wits' ends as to where to get properly conditioned men. Dr. Coca stepped into the breach and organized the service with the aid of a grant from Mr. Rockefeller. When that sum was expended, Dr. Coca turned to the Cornell faculty and the trustees of New York Hospital but they could not give adequate help. Thereupon, Dr. Hartwell laid the whole matter before the Committee on Public Health Relations of the Academy, and Dr. E. H. L. Corwin, then, as now, Secretary of the Committee, was assigned the job of formulating plans. How these eventuated will be gathered from the following extract from the proceedings of the Committee on Public Health Relations of that year, 1929.

"In order to provide the highest possible type of blood donor to the hospitals of Greater New York, and to improve blood transfusion service generally, a group of hospital superintendents of New York City met, at the invitation of the Public Health Relations Committee of The New York Academy of Medicine, and formed a cooperative blood donor organization which was incorporated under the name of 'The Blood Transfusion Betterment Association.' According to the articles of incorporation, the purposes and objectives of the Association are 'The advancement of the science of blood transfusion; the furnishing of voluntary aid, exclusive of medical or surgical service or advice, to persons in need of blood transfusions; the classification of prospective blood donors and collecting information in regard to the same; the studying of the practice of the transfusion of blood in general; the conducting

of investigations, experiments and researches generally to improve blood transfusion; all of these purposes being for the conservation of the public health insofar as it is related to the use of blood transfusion as a therapeutic measure; and the maintaining of a general organization to carry out the above purposes without pecuniary profit.'"

The Association was to be under the control of a Board of Trustees representing the hospitals of the City and The New York Academy of Medicine. A Board of Medical Control was made responsible for the medical policies of the Association, and was composed of representatives from the City Department of Health, the Department of Hospitals, The New York Academy of Medicine, the New York Pathological Association, and the County Medical Societies of New York.

The Report goes on to state that the Association had no endowment at the time and its expenses were to be met through membership fees of hospitals, service charges for donors and voluntary contributions. The Association took over the management of the former Cooperative Donor Bureau operated in connection with the New York Hospital.

For a number of years the offices and laboratories of the Association were housed in an annex of the Academy and it was debated whether the latter should take over the whole administration. This the Council and Trustees decided against as being beyond the function of the Academy. So the Association became an independent body with its own building and organization, giving in this its 21st year ever more and more satisfaction to its proud parent, The New York Academy of Medicine.

From its inception the Association has been interested in the scientific and research phase of its work.

At the time the Blood Transfusion Association was organized, neither the general profession nor the laboratory technicians knew much about the blood grouping tests—how to read them, how to interpret them—nor about how long blood can be stored, nor what is going to happen to the erythrocytes, leukocytes, platelets, plasma, and not much about the preservation of blood, about temperatures, hemolysis, osmotic and mechanical fragility, the techniques of administration, and about the various problems of non-compatibility, the cold agglutinins, etc. All of these and many other problems have been tackled and solved.

One of its notable contributions was the aid and encouragement it gave to Dr. Philip Levine in the elucidation of the clinical aspects of the Rh factor, one of the greatest contributions to knowledge of the blood

since Landsteiner's original work on the major blood groups.

The Association undertook the development of the human Rh testing serum and it was the first to manufacture the other grouping sera on a large scale and to add a dye to differentiate Anti-A from Anti-B grouping sera, thus preventing mistakes, an idea which has since been generally adopted.

In the many thousands of donors tested annually it was found that the strength of the titre varied greatly in different individuals. This led to the use of the blood of these high titred persons for testing purposes. There are many other scientific contributions that could be detailed but time forbids.

It is within the recollection of everyone here that during the Battle of Britain there were sent from this country large supplies of blood plasma to aid the stricken victims. The idea was Dr. Carrel's, and the details were worked out by this Association and The New York Academy of Medicine in cooperation with the Red Cross. It entailed an enormous amount of scientific work and of practical planning which eventuated in supplying to Britain through over 14,000 voluntary donors a total of 5,500 litres of plasma saline solution.

It was this joint effort on the part of the Association, The New York Academy of Medicine, and the Red Cross which set the pattern for the nation-wide blood donation program developed by the Red Cross after this country went to war. We hope and believe that this close liaison will continue in the future, for we are all working for a common cause.

The demand for blood as a therapeutic agent, not only in surgical, but in medical cases goes on increasing. At the present time it is estimated that in New York City an average of four transfusions is being given per hospital bed per year, which means that with the over 40,000 hospital beds in the city we are transfusing 160,000 pints of blood every year. It has been estimated that before long this will reach the fabulous figure of 250,000 pints. The reason for the progressive rise in the demand is that blood transfusion is no longer regarded as something to be resorted to only in dire emergency. It is given very frequently and with enormous advantage in anticipation and in prevention of emergencies in surgical and obstetrical cases. A considerable part of the lowering of maternal mortality in recent years is due to blood transfusions and to the readiness with which blood can be obtained, the precaution being taken in every expectant mother to have her major blood type and Rh factor

determined before the onset of labor.

With this great demand there is need for blood banks in all of our larger hospitals and for community banks and donor bureaus which can supply the smaller hospitals and individual practitioners. It is only through large centers such as this that the rarer blood types are obtainable on short notice.

It should be emphasized that the Blood Transfusion Association has never allowed any commercial tinge to enter into its operations. It is a voluntary non-profit organization directed by a group of doctors and laymen whose only concern is to give efficient service and who reap their reward in the satisfaction of work well done. To them we owe a deep debt of gratitude. It would be impossible to name all of those who have contributed of their time and effort, but I might single out for special mention, Dr. E. H. L. Corwin, who is largely responsible for the early organization and who is still its active and enthusiastic secretary and treasurer. I cannot refrain from mentioning my friend, Mr. John Bush, a member of the original Board of Trustees, and one time President; Dr. John Scudder, one of the pioneers in blood work and still a most prolific worker; and lastly Dr. DeWitt Stetten, the present president whose knowledge, enthusiasm and energy are guaranties for the future.

In declaring this building open I wish the Blood Transfusion Association continuing success in its beneficent work.

LIBRARY NOTES

HISTORICAL MEDICAL TEXTS

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Fracastorius, Hieronymus. De Contagione. Trans. by Wilmer Cave Wright, N. Y., Putnam's, 1930, 356 p. $3.00.

Vesalius, Andreas. Icones Anatomicae. N.Y., 1934. $95.00. Atlas of magnificent folio woodcuts from the original blocks of 1543.

Doe, Janet. A Bibliography of the Works of Ambroise Pare. Chicago, Univ. of Chic. Pr., 1937, 266 p. $5.00.

Ornstein, Martha. The Role of Scientific Societies in the Seventeenth Century. 3.ed. Chic., Univ. of Chic. Pr., 1938, 308 p. $3.00

Van Ingen, Philip. The New York Academy of Medicine: Its First Hundred Years. N.Y., Columbia Univ. Pr., 1949, 586 p. $10.00.

Breasted, James H. The Edwin Smith Surgical Papyrus. Chic., Univ. of Chic. Pr., 1930, 2 vol. $20.00. Beautiful facsimiles with translation and commentary.

Weinberger, Bernhard W. Dental Bibliography. 2.ed. [N.Y., 1929], 2 vol. (262 p.) $2.00. A comprehensive list of the older dental literature.

In Preparation

Three Vesalian Essays to Accompany Vesalius' *Icones Anatomicae* of 1934.

1. Samuel W. Lambert, Sr. on the initial letters.
2. Marginal Notes by the Printer, Willy Wiegand.
3. A discussion of early scientific illustration in general and of the Vesalian woodcuts in particular by William M. Ivins, Jr., former Curator of the Dept. of Prints, Metropolitan Museum of Art.

Lancisi, Giovanni M. De Motu Cordis et Aneurysmatibus. Trans. by Wilmer Cave Wright. An epoch-making contribution to cardiology by the greatest Italian clinician of the 18th century, not heretofore completely rendered into any modern language.

RECENT ACCESSIONS TO THE LIBRARY

("Possession does not imply approval.")

Alexander, F. G. Psychosomatic medicine. N. Y., Norton, [1950], 300 p.

de Allende, I. L. C. & Orías, O. Cytology of the human vagina. N. Y., Hoeber, [1950], 286 p.

Anderson, B. E. The facilitation of interstate movement of registered nurses. Phil., Lippincott, [1950], 186 p.

Anderson, C. M. Saints, sinners and psychiatry. Phil., Lippincott, [1950], 206 p.

Anikin, M. M. & Varshaver, G. S. Osnovy fizioterapii. [Principles of physio-therapy.] 2.izd. Moskva, MEDGIZ, 1950, 711 p.

Anson, B. J. An atlas of human anatomy. Phil., Saunders, 1950, 518 p.

Appleton, A. B.; Hamilton, W. J. & Simon, G. Surface and radiological anatomy. 3.ed. Balt., Williams, 1949, 332 p.

Bayandurov, B. I. Troficheskaya funktsiya golovnogo mozga. [Trophic function of the brain.] Moskva, MEDGIZ, 1949, 306 p.

Beaumont, G. E. Applied medicine. London, Churchill, 1950, 541 p.

Bessey, E. A. Morphology and taxonomy of fungi. Phil., Blakiston, 1950, 791 p.

Biology (The) of human starvation, by A. Keys, J. Brozek, A. Henschel [and others]. Minneapolis, Univ. of Minn. Press, [1950], 2 v.

Blindness; modern approaches to the unseen environment, edited by P. A. Zahl. Princeton, Princeton Univ. Press, 1950, 576 p.

Boyd, W. The pathology of internal diseases. 5.ed. Phil., Lea, 1950, 866 p.

Browne, F. J. Postgraduate obstetrics and gynaecology, 1950. London, Butterworth, 1950, 501 p.

Burrows, H. Biological actions of sex hormones. 2.ed. Cambridge [Eng.] University Press, 1949, 615 p.

Callahan, P. & Callahan, J. T. The law of medicine, N. Y., Oceana Publications, [1950], 80 p.

Carrel, A. The voyage to Lourdes. N. Y., Harper, [1950], 52 p.

Chauchard, P. Le système nerveux sympathique. [Paris], Gallimard, [1949], 364 p.

Chevigny, H. & Braverman, S. The adjustment of the blind. New Haven, Yale Univ. Press, 1950, 320 p.

Colonna, P. C. Regional orthopedic surgery. Phil., Saunders, 1950, 706 p.

Committee for Standardization of Joint Measurements in Industrial Injury Cases. Evaluation of industrial disability. N. Y., Oxford Univ. Press, 1950, 89 p.

Communicable diseases, edited by R. L. Pullen. Phil., Lea, 1950, 1035 p.

Comroe, J. H., jr. & Dripps, R. D. The physiological basis for oxygen therapy. Springfield, Ill., Thomas, [1950], 85 p.

Cowdry, E. V. A textbook of histology. 4.ed. Phil., Lea., 1950, 640 p.

Cummins, S. L. Tuberculosis in history, from the 17th century to our times. London, Baillière, 1949, 205 p.

Doggart, J. H. Ophthalmic medicine. London, Churchill, 1949, 329 p.

Dorcus, R. M. & Shaffer, G. W. Textbook of abnormal psychology. 4.ed. Balt., Williams, 1950, 717 p.

Dyce, J. M. Photographic aids to a clinical dental practice. London, Staples Press, 1948, 175 p.

Eastman, N. J. Williams' obstetrics, 10.ed. N. Y., Appleton-Century-Crofts, [1950], 1176 p.

Epstein, E. H. Regional dermatologic diagnosis. Phil., Lea, 1950, 328 p.

Farris, E. J. Human fertility and problems of the male. White Plains, Author's Press, [1950], 211 p.

Faulkner, R. L. & Douglass, M. D. Essentials of obstetrical and gynecological pathology. 2.ed. St. Louis, Mosby, 1949, 357 p.

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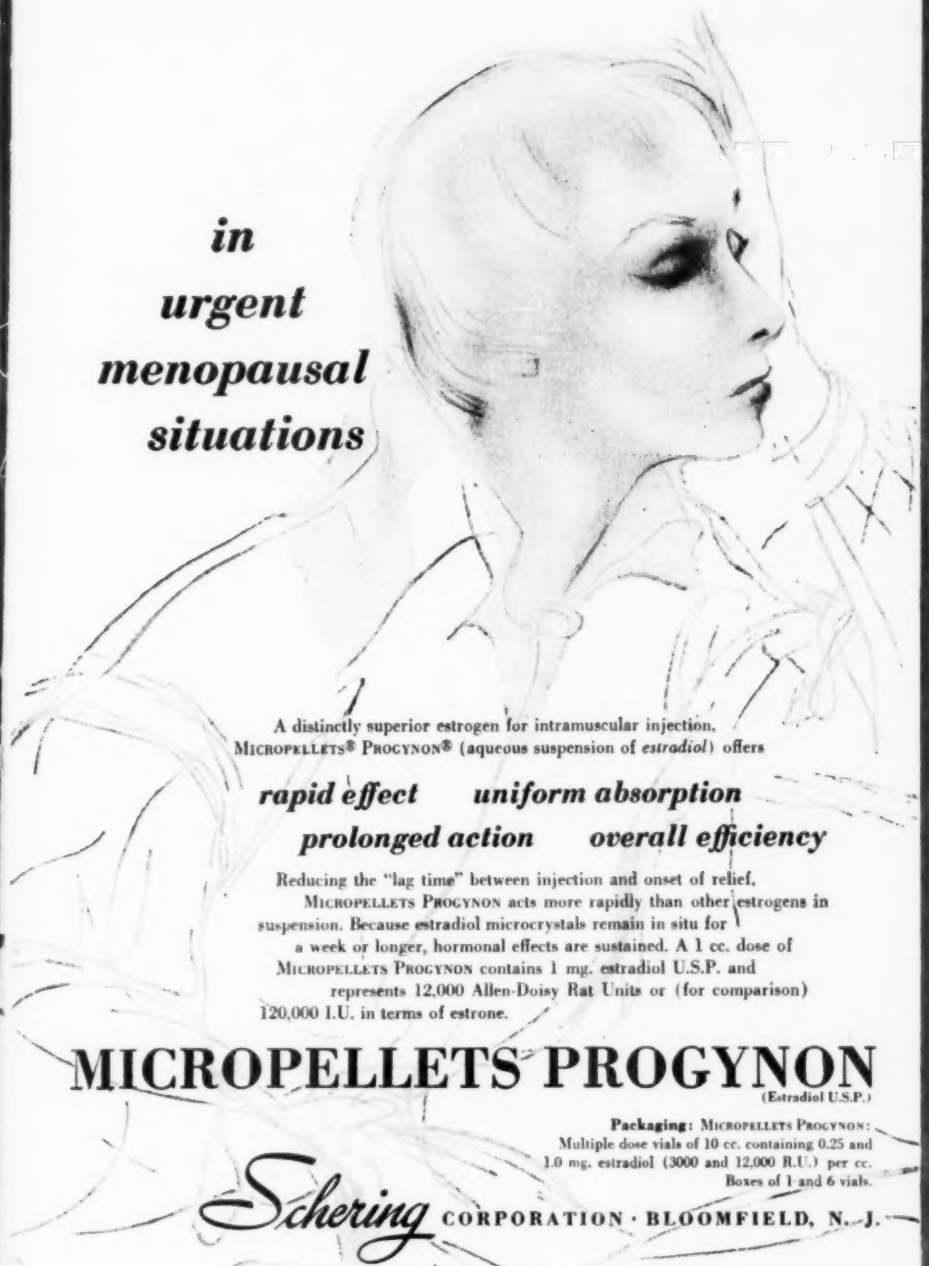

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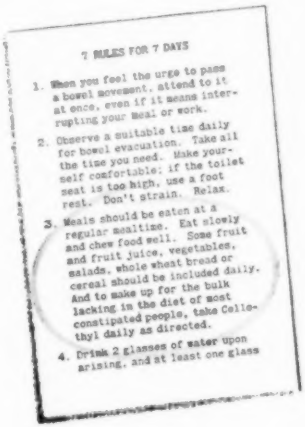

7 RULES FOR 7 DAYS

1. When you feel the urge to pass a bowel movement, attend to it at once, even if it means interrupting your meal or work.
2. Observe a suitable time daily for bowel evacuation. Take all the time you need. Make yourself comfortable; if the toilet seat is too high, use a foot rest. Don't strain. Relax.
3. Meals should be eaten at a regular mealtime. Eat slowly and chew food well. Some fruit and fruit juice, vegetables, salads, whole wheat bread or cereal should be included daily. And to make up for the bulk lacking in the diet of most constipated people, take Cellothyl daily as directed.
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1. "The simple rules of bowel hygiene"[3] are explained and effort is directed against contributory causes[1-3]—faulty diet, cathartic abuse, etc. As a daily reminder of your advice, you may want to give the patient a copy of the leaflet, "7 Rules for 7 Days," which is available on request.

2. Cellothyl (physiologically correct colloid) is prescribed, 3 tablets t.i.d., each dose with a full glass of water to assure proper hydrophilic action.

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1. Bargen, J. A.: Gastroenterology *13*:275, 1949.
2. Musick, V. H.: J. Oklahoma M. A. *43*:560, 1950.
3. Schweig, K.: New York State J. Med. *48*:1822, 1948.
4. Council on Pharmacy and Chemistry: J.A.M.A. *143*:897, 1950.

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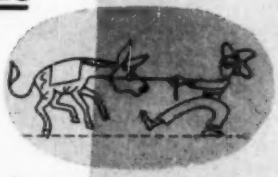

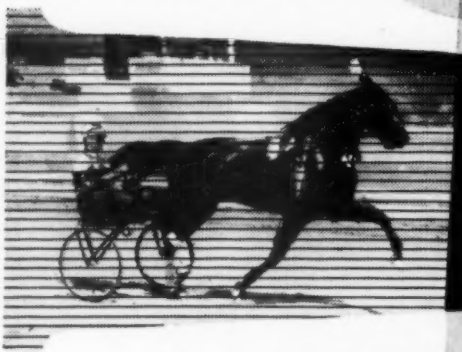

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1. Behrman, H. T., Combes, F. C., Bobroff, A., and Leviticus, R.: Ind. Med. & Surg. 18:512. 1949.

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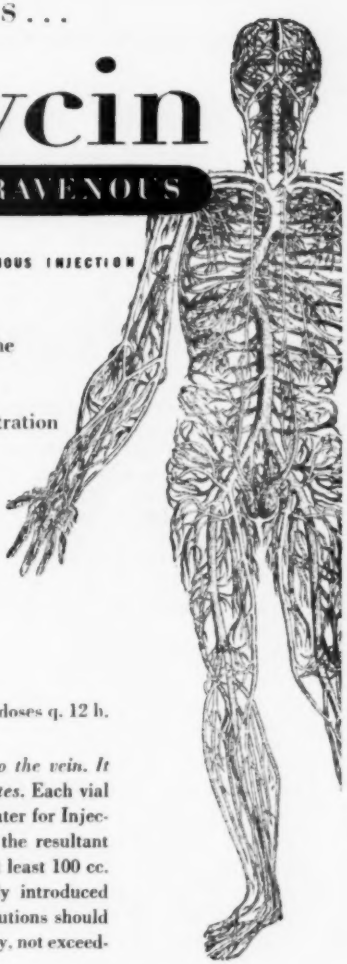

Affords the advantages of intravenous therapy with the newest of the broad-spectrum antibiotics in:

... those conditions and cases in which oral administration is not feasible;

... severe, fulminating or necrotizing infections (by rapidly producing high serum concentrations);

... pre- and post-operative prophylaxis;

... peritonitis.

Dosage and Administration:

0.5 Gm. to 1.0 Gm. of Terramycin Intravenous in divided doses q. 12 h. has been found adequate for most acute infections.

Terramycin Intravenous should be injected directly into the vein. It is never given by the intramuscular or subcutaneous routes. Each vial is dissolved in sterile 5% Dextrose for Injection, USP, Water for Injection, USP, or Physiological Saline Solution, USP, and the resultant clear solution further diluted to give a final volume of at least 100 cc. When desired, Terramycin Intravenous may be directly introduced into solutions for continuous drip infusion. Injection solutions should not contain more than 5 mg. per cc. and are injected slowly, not exceeding 100 cc. in five minutes.

Supplied: 10 cc. vials containing 250 mg. of Crystalline Terramycin Hydrochloride with sodium glycinate as a buffer.
20 cc. vials containing 500 mg. of Crystalline Terramycin Hydrochloride with sodium glycinate as a buffer.

Antibiotic Division Pfizer CHAS. PFIZER & CO., INC., *Brooklyn 6, N. Y.*

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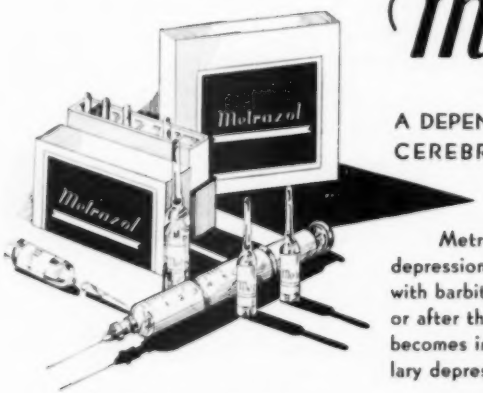

Metrazol, pentamethylentetrazol
Ampules, 1 cc. and 3 cc.
Sterile Solution, 30 cc. vials
Tablets and Powder

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Metrazol is indicated in narcotic depression, for instance, in poisoning with barbiturates or opiates and during or after the operation when respiration becomes inadequate because of medullary depression due to the anesthetic.

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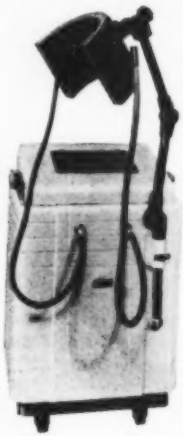

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A Penicillin-Resistant Bacteremia[1]

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History C. D., female, age 2
Illness of 5 days' duration; temp. 103.6° F.; blood culture positive for S. cholerae-suis, var. Kunzendorf; previous treatment with penicillin without response.

Therapy Terramycin, 3 Gm. daily for 12 days; orally in divided doses q. 4 h.

Result Temp. to normal in 24 hours. Response described as "excellent".

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1. Terramycin may be highly effective even when other antibiotics fail.[1]
2. Terramycin may be well tolerated even when other antibiotics are not.[2]

Suggested for: *acute pneumococcal infections, including lobar pneumonia, bacteremia; acute streptococcal infections, including erysipelas, septic sore throat, tonsillitis; acute staphylococcal infections; bacillary infections, including anthrax; urinary tract infections due to E. coli, A. aerogenes, Staphylococcus albus or aureus, and other Terramycin-sensitive organisms; acute brucellosis (abortus, melitensis, suis); hemophilus infections; acute gonococcal infections; lymphogranuloma venereum; granuloma inguinale; primary atypical pneumonia; typhus (murine, epidemic, scrub); rickettsialpox.*

Dosage: 2 to 3 Gm. daily by mouth in divided doses q. 6 h. is suggested for acute infections.

Supplied: 250 mg. capsules, *bottles of 16 and 100;*
100 mg. capsules, *bottles of 25 and 100;*
50 mg. capsules, *bottles of 25 and 100.*

1. King, E. G.; Lewis, C. H.; Welch, H.; Clark, E. A., Jr.; Johnson, J. B.; Lyons, J. B.; Scott, R. B., and Connely, P. B.: J. A. M. A. 143:1 (May 6) 1950.

2. Herrell, W. E.; Hoffman, F. R.; Wellman, W. E., and Bartholomew, L. A.: Proc. Staff Meet. Mayo Clin. 25:183 (Apr. 12) 1950.

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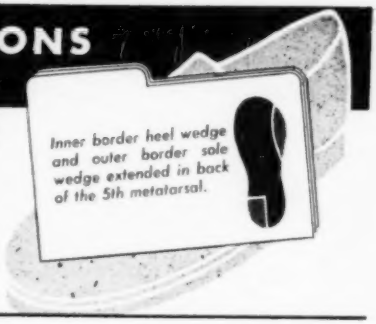

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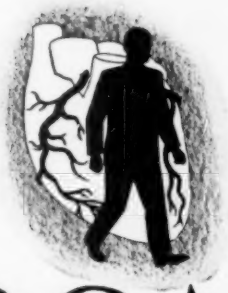

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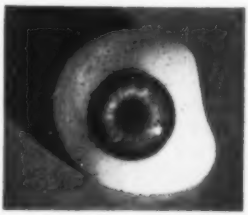

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BANANA RYE BREAD
(Egg, milk and wheat free)

2 cakes or packages yeast
¼ cup warm (not hot) water
1 tablespoon salt
1½ tablespoons sugar
2 tablespoons melted vegetable shortening
2¼ cups mashed ripe bananas* (5 to 6 bananas)
5¼ to 6 cups rye flour

**Use fully ripe bananas . . . yellow peel flecked with brown.*

Dissolve yeast in water. Mix together salt, sugar, shortening and bananas. Add half the flour and beat until smooth. Beat in the dissolved yeast. Add remaining flour gradually and mix well.

Turn dough out onto a floured board. Knead about 8 minutes, adding just enough additional rye flour to prevent sticking. Place dough into a lightly greased bowl. Cover and let rise until double in bulk (about 2 hours).

Turn out again onto floured board and knead lightly about 2 minutes. Shape dough into 2 loaves. Place into lightly greased bread pans (8 x 4 x 3 inches). Cover and let rise again until double in bulk (about 1 hour).

Bake in a hot oven (425° F.) 5 to 10 minutes, or until crust begins to brown. Reduce temperature to 350° F. and bake 35 to 40 minutes longer, or until bread is done. Remove from pans. Brush top crusts with water. Makes 2 loaves.

All measurements used in this recipe are level.

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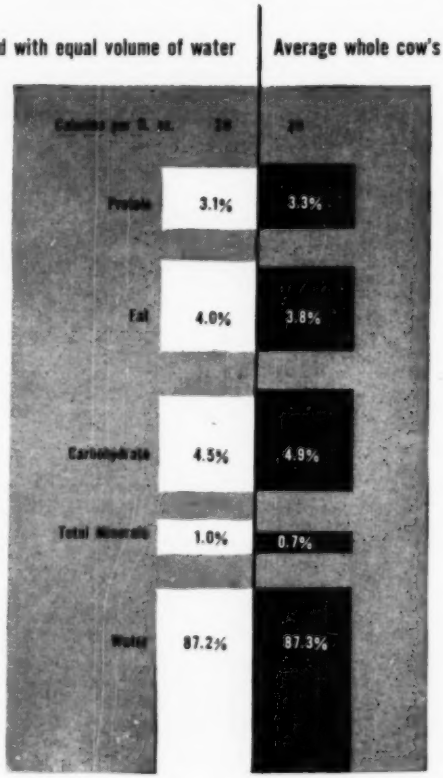

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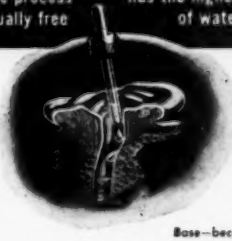

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. . . a potent chemical combination (*not a mere mixture*), combining Sulfathiazole and Urea in AURALGAN Glycerol (DOHO) Base—because it exerts a powerful solvent action on protein matter, liquefies and dissolves exuberant granulation tissue, cleanses and deodorizes, and tends to exhilarate normal tissue healing in the effective control of chronic suppurative otitis media.

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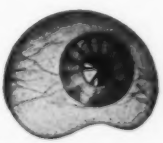

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And along with millions of others, convalescents are sure to enjoy the lighter, cleaner taste of this fine *Premium* Beer.

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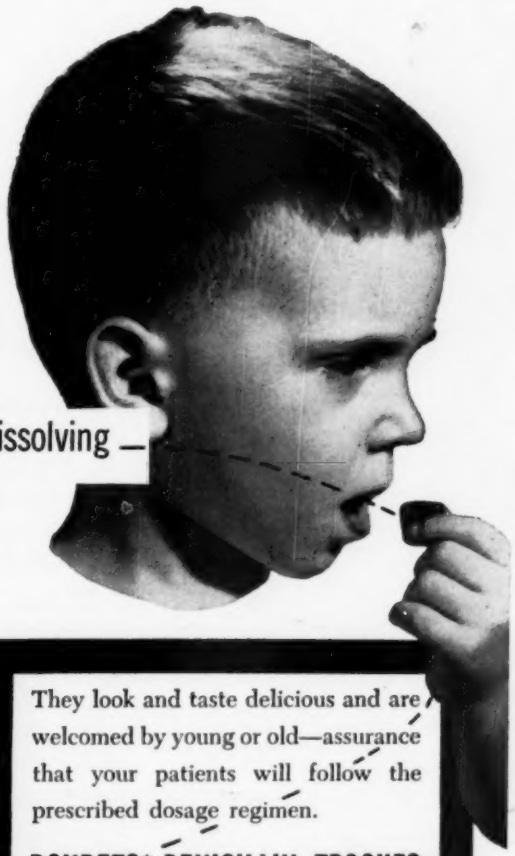

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—Hardesty, L. M. and Gonzalez, W. *J.*
Am. Heart J., 38:477 (Sept. 1949).

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